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Original Communications

CREATION OF A TEMPORARY ARTIFICIAL DUCTUS FOR THE SURGICAL CORRECTION OF VENTRICULAR SEPTAL DEFECTS ASSOCIATED WITH SEVERE PULMONARY HYPERTENSION

A Two-Stage Operation

Howard D. Sirak, M.D. (by invitation), and Don M. Hosier, M.D. (by invitation), Columbus, Ohio

When an interventricular septal defect is associated with severe pulmonary hypertension, surgical correction has resulted in a high operative mortality. In Lillihei's series of patients over 2 years of age in whom the pulmonary artery systolic pressure was 70 per cent or more of the aortic systolic pressure, the operative mortality has been reported as 37 per cent.[1] In those cases, in which the pressures in the two systems are essentially equal, the mortality has been even greater.[2, 3, 4] However, it will be recalled that most young children with an atypical ductus and equal-pressure pulmonary hypertension have tolerated surgical closure.[5 6] A possible explanation for this difference in results is that, in the case of interventricular septal defect, the cardiovascular system cannot withstand the combined burdens of open-heart surgery and those imposed by the physiologic readjustment to defect closure. Therefore, it seemed worth while to try to lower operative mortality by preventing these two major burdens

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From the Department of Surgery (Cardiovascular Service) and the Pediatric Cardiology Service, The Ohio State University Health Center and the Children's Hospital, Columbus, Ohio

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from coinciding in one operation. Accordingly, a two-stage operation was devised for those children with ventricular septal defects in whom the systolic pressures in the pulmonary artery and aorta were essentially equal. The first stage consists of establishing a temporary ductus between the ascending aorta and the pulmonary artery and closing the interventricular septal defect. At the second stage, performed 3 to 6 months later, after the heart and lungs have recovered from the operative manipulation, the artificial ductus is divided. In this manner, the final correction, which imposes the severest physiologic burden, is accomplished by a lesser operative undertaking.

OPERATIVE PROCEDURE

The patient is prepared for open-heart surgery* in the usual fashion: He is placed on the table in the supine position, both common femoral arteries are isolated between umbilical tapes, and the chest opened bilaterally via a transverse transsternal incision through the fourth interspace. The pericardium is incised transversely and then parallel to the right phrenic nerve and retracted with the sternum. The ascending aorta is dissected free and encircled with an umbilical tape. The superior (central to the azygos vein) and inferior venae cavae are doubly encircled with siliconed umbilical tapes.

The First Stage.—At a site about 1½ to 2 cm. from the base of the aorta, its anteromedial surface is cleaned of adventitia as is a corresponding area on the right anterolateral aspect of the main pulmonary artery. A portion of the aortic—and then the pulmonary artery—lumen is isolated for anastomosis by means of a curved vascular clamp. An elliptical piece of tissue is removed from each vessel wall; otherwise, if the anastomosis is done to a longitudinal slit, thrombosis of the graft is prone to occur. A graft, with an inside diameter of approximately 10 mm., is then anastomosed in end-to-side fashion employing a continuous 5-0 arterial silk (Fig. 1). The aortic clamp is left in place until the pulmonary artery anastomosis is completed. To prevent kinking of the graft, both ends should be cut obliquely.

Several types of graft materials have been employed. Nylon grafts (Edwards-Tapp) have been tried, but are no longer used because hemostasis at the suture lines may become troublesome after the patient is heparinized and, more important, the ends cannot be conveniently tailored inside the chest. Aortic homografts were found to be most suitable at the time of the first stage, but imposed a difficult technical problem at the second stage because more operative exposure was needed to permit placing the sutures directly in the walls of the aorta and pulmonary artery. It would be inadvisable simply to close the divided ends of the homograft lest future rupture occur. Both of these requirements can be met by putting a 1.5 cm. sleeve of seamless Dacron cloth tubing† over each end of a child's aortic homograft of appropriate diameter and incorporating it in the anastomosis.

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*Kay-Cross Oxygenator, manufactured by Pemco, Inc., Cleveland.

†Available from John B. Sidebotham, Inc., 4317 Griscom Street, Frankford, Philadelphia 24, Pa.

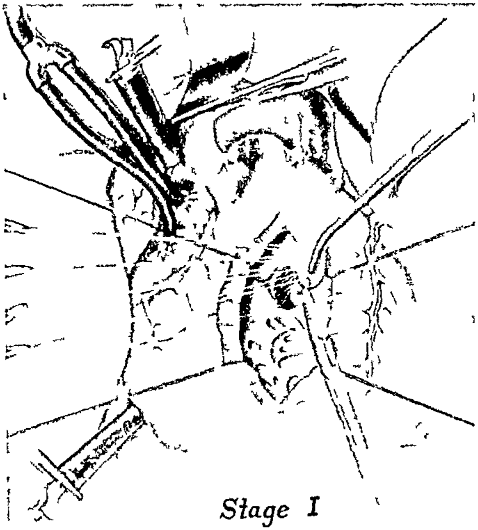

Fig 1.—Stage One Open heart procedure The artificial ductus is placed between the ascending aorta and main pulmonary artery The septal defect is closed employing potassium citrate arrest

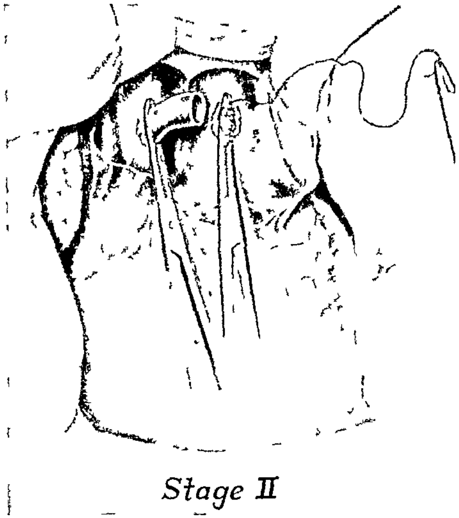

Fig. 2.—Stage Two Three to 6 months later the temporary 'ductus is divided and over sewn close to each great vessel

Upon completing both anastomoses, the pulmonary artery clamp is removed, gradually at first, until the suture lines cease leaking. The aortic clamp is then removed. After the operator is satisfied with the hemostasis, the patient is heparinized (3 mg./Kg. body weight) and then cannulated for the extracorporeal bypass. During the bypass, the graft is occluded with a bulldog clamp. Elective cardiac arrest, with the aorta cross-clamped distal to the graft site, is used during the repair of the defect. If the defect is large (over 1 cm.), a double-thickness Teflon cloth* patch is sewn in place employing mattress sutures of atraumatic 3-0 Dacron.† If it is smaller, the sutures are passed through and tied over a cigarette-shaped pledget of Ivalon sponge. The aortic clamp is removed and, when adequate heart action has returned, the ventricular incision is repaired. The bulldog clamp on the graft is removed after the vena caval tourniquets have been loosened and the pump-oxygenator perfusion rate has been cut back to about 30 per cent of its original level. The patient is decannulated and protamine is injected. The anastomoses are again inspected for hemostasis, after which the pericardium is loosely closed over the graft.

Stage II.—The child is placed in the supine position with the right side elevated about 30 degrees. The right-sided portion of the previous skin incision is excised and the chest entered through the third interspace. The adherent lung and pericardium are dissected away from the mediastinum in the area of the graft which can now be palpated. The graft is cross-clamped, divided, and closed with sutures. The suturing is placed as close to each great vessel as possible incorporating both the homograft and the Dacron cloth sleeve (Fig. 2).

CASE REPORTS

CASE 1.—D. L., a 3-year-old boy who previously had had multiple operations for other congenital defects including pyloric stenosis, cleft palate, and inguinal hernia, was admitted for evaluation of a heart murmur that had been recognized since birth. His parents stated that he had repeated respiratory infections and his exercise tolerance was limited.

The child placed below the third percentile on the growth chart. On auscultation a Grade 2 (1-4) systolic murmur was heard along the left sternal border, being loudest in the third left intercostal space near the sternum. This murmur was not widely transmitted. P_2 was loud and snapping and a faint short diastolic murmur was present in the pulmonic area.

The electrocardiograph showed right and left ventricular enlargement (Fig. 3). The teleoroentgenogram demonstrated cardiac enlargement and increased pulmonary vascular markings (Fig. 4). On fluoroscopy, the activity of the pulmonary arteries was found to be moderately increased over normal. Cardiac catheterization done on Jan. 29, 1957, under morphine and Nembutal sedation, disclosed equal pressures in the greater and lesser circulations (Table I). The catheter passed through a ductus into the aorta. The next day blood samples were obtained simultaneously from the right brachial and femoral arteries. A differential in saturation of the samples was noted (Table I). A diagnosis was made of interventricular septal defect and patent ductus arteriosus with equal-pressure pulmonary hypertension and predominant left-to-right shunt at the septal defect with some reversal of flow through the ductus. The child was discharged to await scheduling for open-heart surgery.

The child was readmitted for the first part of a two-stage operation. On May 17, 1957, the ductus, which was very short and about 5 mm. in diameter, was first isolated and temporarily occluded with an umbilical tape. The patient was then cannulated for extracorporeal bypass. The interventricular septal defect was 12 mm. in diameter and, employing potassium citrate arrest, a double thickness patch of Teflon cloth was sewn in place, using interrupted mattress sutures of 3-0 atraumatic Dacron. As the bypass was being discontinued, the tourniquet on the ductus was released During the early postoperative period, difficulty with secretions necessitated a tracheotomy.

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*Available from John V. Sidebotham, Inc., 4317 Griscom Street, Frankford, Philadelphia 24, Pa.

†Supplied by Mr. C. W. Norman, Ethicon, Inc., Somerville, N. J.

This patient was again admitted approximately 6 months later. He had gained weight and his color had improved A systolic murmur could be heard over the left second interspace The electrocardiograph showed some regression of the right ventricular hypertrophy pattern

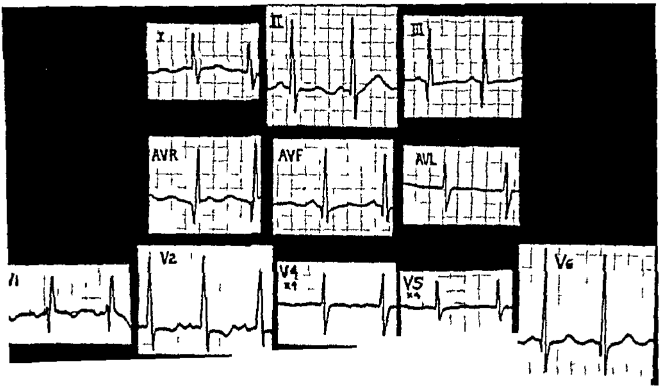

Fig 3.—Case 1 Preoperative electrocardiograph showing an incomplete right bundle branch block with a tall R wave in aVr indicating right ventricular hypertrophy The tall R wave in V_5 and V_6 is evidence of left ventricular hypertrophy (Paper speed 50 mm./sec.)

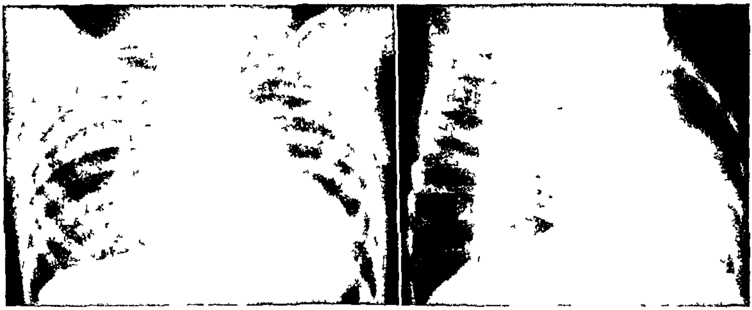

Fig 4.—Case 1 Chest roentgenograms (PA and RAO) demonstrating cardiac enlargement prominent pulmonary conus and accentuated hilar vascular markings

On fluoroscopy, the hilar activity still appeared to be accentuated An attempt at catheterization was unsuccessful On Dec 18, 1957, through a left posterolateral incision, the ductus was redissected and divided The patient made an uneventful recovery

The child was readmitted to the hospital on Feb 20, 1958, 3 months after the second stage for cardiac catheterization The data showed a marked regression in pressures and normal saturation values (Table I).

Comment: The fact that the pressures had returned to the upper limits of normal (with the patient sedated) just 3 months after the second stage tends to corroborate the large role played by the flow-factor in this patient. It would be reasonable to assume that the vascular changes present in the lung (Fig. 5) certainly could not have had time to regress completely; thus, one might infer that there was still a reduction in wall:lumen ration, but that ample capacity remained once the excess flow was removed. Therefore, the "temporary"

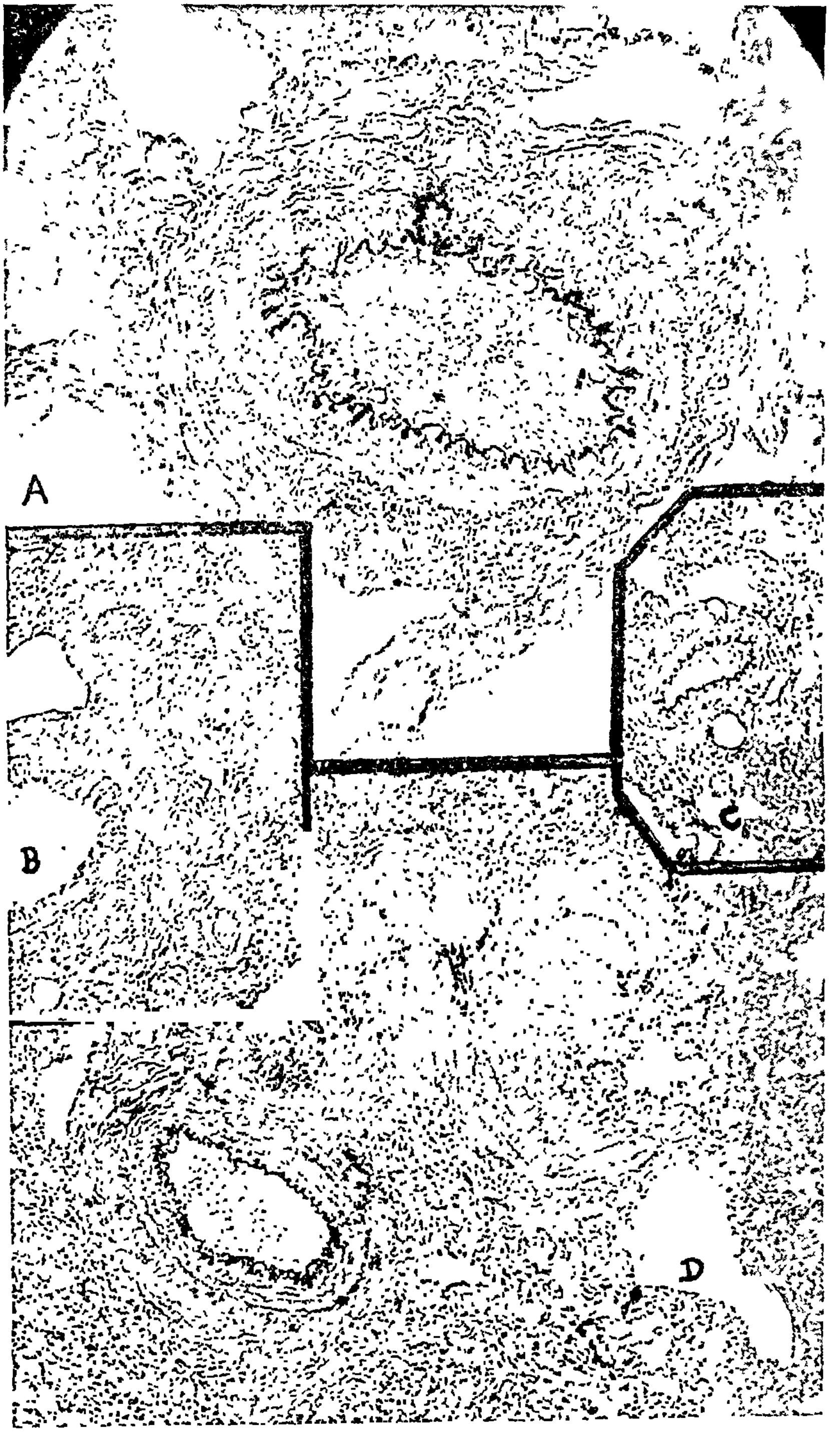

Fig. 5.—Case 1. Photomicrograph of the lung biopsy obtained at the first stage showing moderately severe changes in the small muscular arteries. *A*, × 225; *B*, *C*, and *D*, × 100.

ductus may have aided the immediate postoperative recovery from the open-heart surgery by compensating for the effects of a possible superimposed functional pulmonary vascular component. The latter might be initiated by the alteration of the pulmonary blood flow and the manipulation of the heart and lungs.

TABLE I

D. L.	PREOPERATIVE		AFTER CLOSURE OF DUCTUS	
	SATURATION PER CENT	PRESSURE (MM. HG)	SATURATION PER CENT	PRESSURE (MM. HG)
Superior vena cava	66.5		69.5	
Right atrium	68	7	70	4
Right ventricle	83	80/0	69	35/0
Pulmonary artery	83.5	80/35	70.5	34/9
Aorta	93	80/46		
Right femoral artery	90*		90	64/36
Right brachial artery	98*			

Case 1. Cardiac catheterization data obtained before the first stage demonstrated an interventricular septal defect and a patent ductus arteriosus with equal-pressure pulmonary hypertension. There is a 15 per cent step-up in saturation of the right ventricular sample. The catheter passed through the patent ductus into the aorta. Simultaneous samplings of the right brachial and femoral arteries indicated flow reversal through the ductus. Two months after the second stage, on repeat catheterization, the saturations had returned to normal, and the pulmonary artery pressures had regressed toward normal. The low systemic arterial pressure suggests that the pulmonary artery pressure may actually be higher than the figures indicate.

*Simultaneous preoperative studies done without sedation

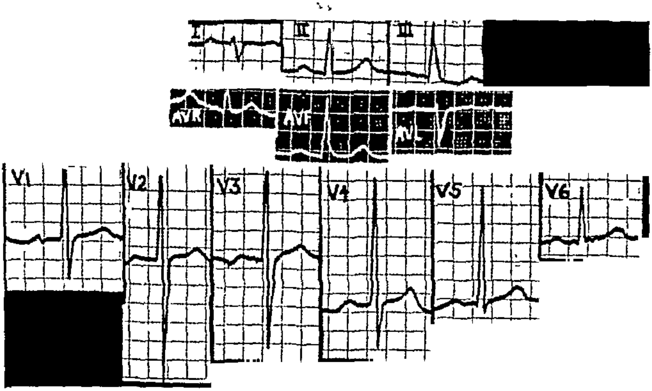

Fig 6.—Case 2. Preoperative electrocardiogram showing right ventricular hypertrophy. The tall R wave in V_5 suggests some left ventricular hypertrophy. (Paper speed, 50 mm./sec.)

CASE 2.—D. K., a 4½-year-old girl, was referred for correction of a cleft palate. On examination, a heart murmur was detected, and a cardiac consultation was obtained. The child placed below the third percentile on the growth chart. There was a slight left precordial bulge and a faint thrill could be palpated over the third and fourth intercostal spaces. A coarse Grade 2 (1-4) systolic murmur was present along the left sternal border, being maximal in the fourth left intercostal space near the sternum. P_2 was markedly accentuated.

The electrocardiograph showed evidence of both right and left ventricular hypertrophy (Fig. 6). A teleoroentgenogram (Fig. 7) demonstrated enlargement of the heart with increased pulmonary vascular markings. On fluoroscopy, pulsations of the pulmonary arteries were considered to be moderately increased over normal. Cardiac catheterization was performed (Table II) and a diagnosis was made of interventricular septal defect with equal-pressure pulmonary hypertension with significant left-to-right shunt.

The child was discharged and readmitted at a later date. On July 17, 1957, the first-stage operation was undertaken. Exclusion clamps were placed on the ascending aorta and pulmonary artery, the wall of each was incised longitudinally, and a nylon graft (Edwards-Tapp), 3/16 inch inside diameter, was sewn in place. After the bypass was established, a 15 mm. septal defect was closed employing a double-thickness Teflon cloth patch. When the bypass was discontinued, the patient's heart seemed incapable of maintaining an adequate

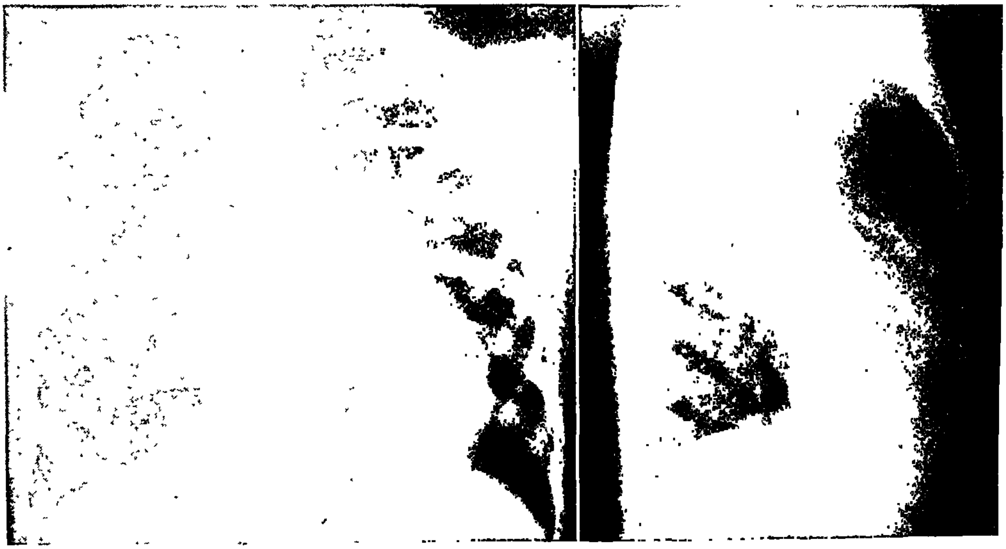

Fig. 7.—Case 2. PA and right lateral chest roentgenograms showing cardiac enlargement and prominent hilar vascular markings.

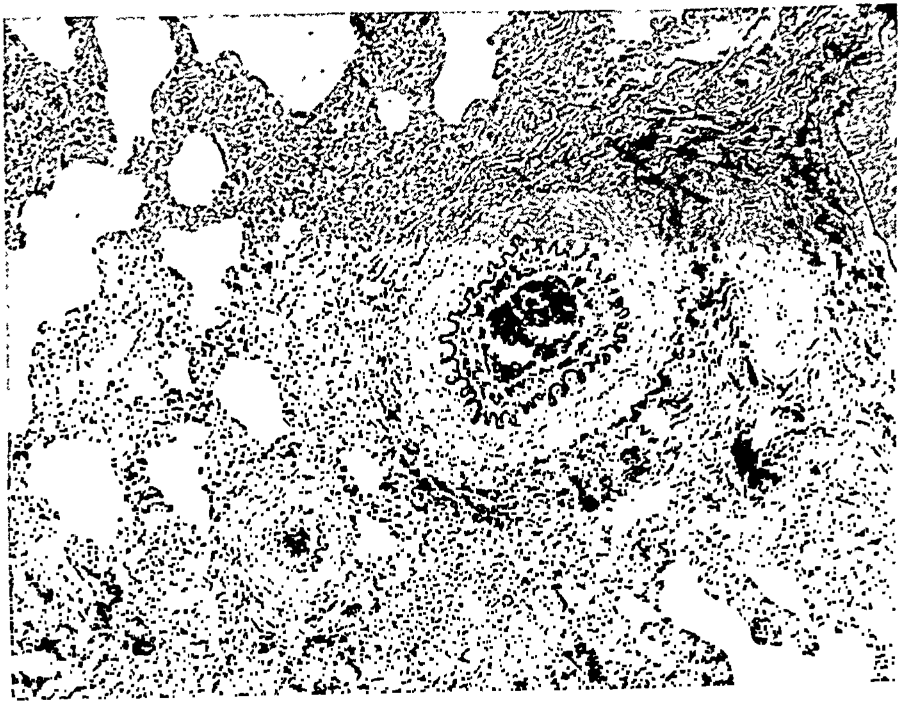

Fig. 8.—Case 2. Photomicrograph of tissue obtained from a central area of the lung showing moderately severe medial hypertrophy of the small muscular arteries. (X 90.)

TABLE II

D K	PREOPERATIVE	
	SATURATION PER CENT	PRESSURE (MM HG)
Inferior vena cava	78	
Right atrium	76	7
Right ventricle	86	84/0
Pulmonary artery	88	86/35
Femoral artery	96	90/60

Case 2 Preoperative catheterization diagnostic of interventricular septal defect with equal pressure pulmonary hypertension There is about a 10 per cent step up in the right ventricular sample

circulation A thrill could not be palpated in the main pulmonary artery opposite the anastomosis The child's condition remained precarious and she died 30 minutes after completion of the chest closure

Comment The graft employed in this patient was much too small and the anastomoses were not satisfactory, having been done to longitudinal incisions in the aorta and pulmonary artery It is believed that due to these two technical errors there was probably no flow across the graft and therefore it did not fulfill its intended function The adverse behavior of the child's circulatory system, commencing shortly after the pump was turned off, is characteristic of this group of patients

The photomicrograph of lung tissue obtained at autopsy demonstrates moderately severe vascular changes (Fig 8)

CASE 3 —M F, a small 5 year old girl, was admitted for evaluation of a heart murmur A systolic thrill was palpable along the left sternal border A harsh, blowing Grade 3 (1 4) systolic murmur could be heard along the left sternal border Although it was maximal in the fourth left intercostal space near the sternum, it was transmitted over the entire precordium P_2 was markedly accentuated

An electrocardiograph (Fig 9) demonstrated an incomplete right bundle branch block with evidence of both right and left ventricular hypertrophy Teleoroentgenograms (Fig 10) showed an enlarged heart with an increase in the pulmonary vascular markings On fluoroscopy, the pulsatile activity of the pulmonary arteries appeared to be moderately increased Cardiac catheterization was performed and a diagnosis of interventricular septal defect with equal pressure pulmonary hypertension and significant left to right shunt was made (Table III)

TABLE III

M F	PREOPERATIVE		AFTER CLOSURE OF DUCTUS	
	SATURATION PER CENT	PRESSURE (MM HG)	SATURATION PER CENT	PRESSURE (MM HG)
Inferior vena cava				
Right atrium	69	6	72	3 5
Right ventricle	74	82/0	68 5	26/0
Pulmonary artery	76	80/34	66	24/7
Femoral artery	85	86/40	100	94/56

Case 3 The preoperative catheterization demonstrates an interventricular septal defect with equal pressure pulmonary hypertension There is about a 5 per cent step up in the right ventricular sample The desaturation of the femoral sample may have been influenced by sedation Recatheterization 6 months later shows a return to normal hemodynamics

The patient was readmitted at a later date for the first of the two stage procedure A ⅜ inch, inside diameter, Edwards Tapp graft was placed between the ascending aorta and the pulmonary artery An elliptical piece of vessel wall was removed at each anastomotic site *The bypass was then established and an 8 mm septal defect was closed with three 3 0* atraumatic Dacron sutures After the bypass was discontinued, a strong thrill could be palpated in the pulmonary artery opposite the "ductus" A tracheotomy was performed

The child made an uneventful recovery. A systolic shunt murmur could be heard over the upper portion of the sternum until the tenth postoperative day when it disappeared. It was suspected that the graft had become clotted. The child continued to do well and was discharged home on the fourteenth postoperative day after the tracheotomy wound had healed.

This patient was again admitted in January, 1958, 6 months following the surgery, for recatheterization. The shunt murmur was still absent. The data showed that the saturations and pressures had returned to normal (Table III).

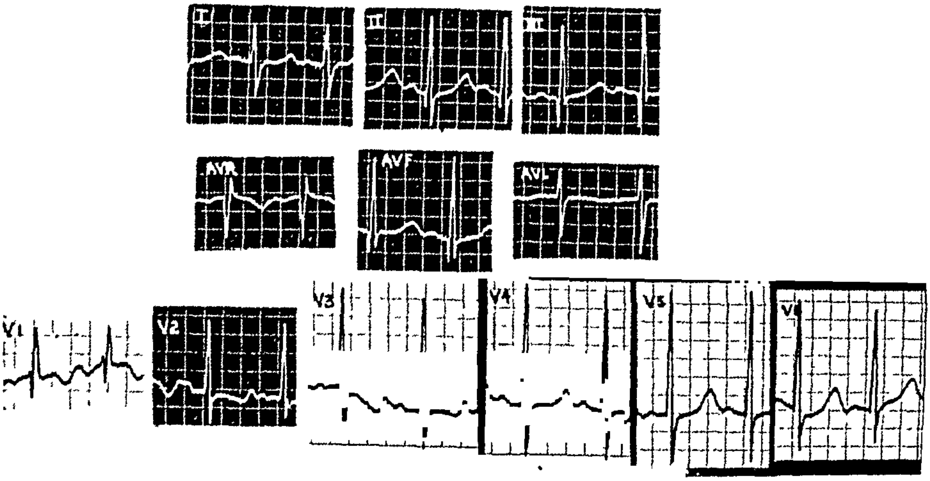

Fig. 9.—Case 3. Preoperative electrocardiograph showing an incomplete right bundle branch block with evidence of enlargement of both ventricles. (Paper speed, 50 mm./sec.)

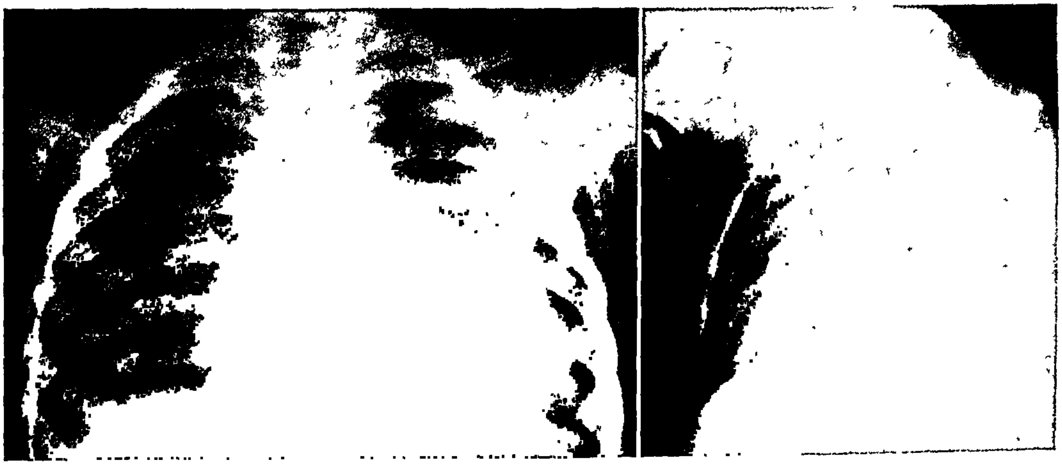

Fig. 10.—Case 3. PA and LAO chest roentgenograms showing cardiac enlargement and accentuated hilar vascular markings. The film was taken during expiration which exaggerates the transverse diameter of the heart.

Comment: The step-up of only 6 per cent in the preoperative right ventricular catheterization sample points to a rather small shunt across the defect; perhaps this explains why the graft ultimately became clotted. This was confirmed by recatheterization. It was very gratifying to note that the pressures and saturations in the right ventricle and pulmonary artery had all returned to normal values. The smooth postoperative course in this patient suggests that the shunt-graft may be needed only during the very early postoperative period and that, after this time, there is adequate recovery from the ventricular incision and the bilateral thoracotomy so that its function was no longer necessary. On the other hand, it may mean that this was one patient who would have tolerated a one-stage correction. However, we were unable to discover anything different in the clinical findings or laboratory data which would have helped us preoperatively to distinguish it from the other cases of its kind.

CASE 4.—N. W., a 5 year old girl, was admitted for evaluation of a heart murmur. The child was below the third percentile on the growth chart. A systolic thrill was palpated over the third and fourth left intercostal spaces near the sternum. A harsh, blowing Grade 3 (1-4) systolic murmur was heard loudest in the same area and was transmitted over the entire left chest. P_2 was loud and snapping.

An electrocardiograph (Fig. 11) showed an incomplete right bundle branch block with evidence of both right and left ventricular hypertrophy. A teleoroentgenogram (Fig. 12) demonstrated an enlarged heart and accentuated pulmonary vascularity. On fluoroscopy, the activity of the pulmonary arteries was found to be moderately increased. Cardiac catheterization was performed (Table IV). A diagnosis of ventricular septal defect with equal pressure pulmonary hypertension and significant left to right shunt was made.

TABLE IV

N. W.	PREOPERATIVE	
	SATURATION PER CENT	PRESSURE (MM. HG)
Superior vena cava	70	
Right atrium	69	7
Right ventricle	76	82/0
Pulmonary artery	78	85/40
Femoral artery	85	90/50

Case 4. Preoperative catheterization studies were diagnostic of an interventricular septal defect with equal-pressure pulmonary hypertension. There was an 8 per cent step-up in the right ventricular sample. The desaturation of the femoral artery sample may be due to sedation.

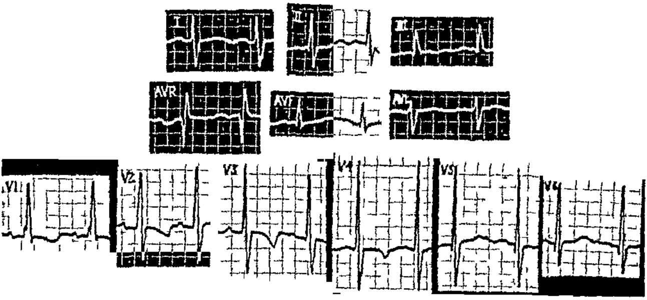

Fig. 11.—Case 4. Preoperative electrocardiograph showing right ventricular hypertrophy and evidence of some left ventricular enlargement. (Paper speed 50 mm./sec.)

On Aug. 7, 1957, the child was readmitted for the first stage of the two stage operation. A homograft, 10 mm. in inside diameter, was inserted between the aorta and the pulmonary artery. An elliptical piece of vessel wall was removed from each great vessel. Each end of the graft was cut obliquely. The bypass was instituted and an 8 mm. septal defect was repaired with several atraumatic 3-0 Dacron sutures. A tracheostomy was performed. The patient made an uneventful convalescence. Postoperatively, a loud systolic murmur could be heard over the upper end of the sternum.

The child was readmitted 3 months later for the second stage operation. The loud shunt murmur was still present over the upper end of the sternum. The right chest was reopened through a portion of the previous incision. The lung and pericardium were dissected away from the area of the temporary "ductus." Because a homograft had been employed, it was deemed necessary, after dividing the shunt, to place the sutures directly in the wall of the pulmonary artery and aorta. In order to gain adequate exposure of the pulmonary anastomotic site, the sternum had to be transected, but the left pleural space was not entered. The child made an uneventful recovery.

Comment: The postoperative course of this patient following the first stage was strikingly smooth. This supported our belief in the importance of employing a large diameter graft in order to be assured of sustaining an ample left-to-right shunt. Her recovery from the second stage was similarly uneventful. She will be recatheterized again at a later date.

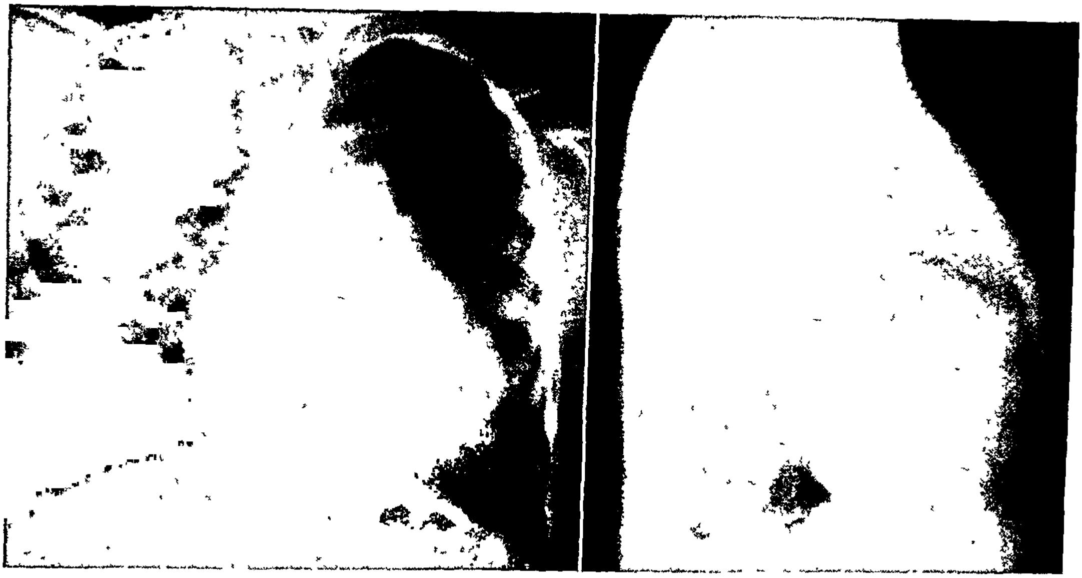

Fig. 12—Case 4. PA and right lateral chest roentgenograms showing cardiac enlargement and accentuated hilar vascular markings.

CASE 5.—J. S., an 11-year-old boy, who had previously been treated for a brain abscess, was readmitted for evaluation of a heart murmur noted during the first admission. The parents reported that he readily became tired on exertion and that at times his lips became blue.

A soft, Grade 1 (1-4) systolic murmur could best be heard in the fourth left intercostal space near the sternum. P_2 was very loud and snapping.

The hemoglobin was 15.7 grams. The electrocardiogram (Fig. 13) showed only a right ventricular hypertrophy pattern. A teleoroentgenogram demonstrated the heart size to be within normal limits with an increased prominence of the pulmonary conus and pulmonary arteries extending to about the mid-lung area (Fig. 14). However, the peripheral vascular markings were not considered to be increased over normal. On fluoroscopy, the pulsations of the pulmonary arteries were demonstrated to be only minimally increased over normal. Cardiac catheterization was performed (Table V). A diagnosis was made of interventricular septal defect with equal-pressure pulmonary hypertension with minimal left-to-right shunting and beginning reversal of flow.

TABLE V

	PREOPERATIVE	
J. S.	SATURATION PER CENT	PRESSURE (MM. HG)
Superior vena cava	78	
Right atrium	79	6
Right ventricle	82	82/0
Main pulmonary artery	84	84/40
Brachial artery	92	86/56

Case 5. Preoperative catheterization studies indicating a small left-to-right shunt at the ventricular level and equal-pressure pulmonary hypertension. This was not increased by the inhalation of oxygen. The peripheral arterial sample (when coupled with other data) may indicate early flow-reversal because the patient was not sedated.

It was recognized that the vascular changes in this patient were much more marked than in any of the previous patients The parents were apprised of our grave forebodings, but they wished the child to be given every opportunity Accordingly, the child was discharged to be scheduled for open heart surgery at a later date

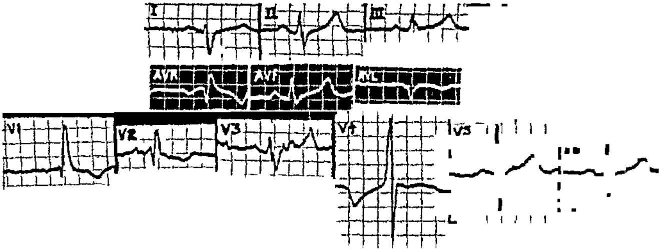

Fig 13—Case 5 Preoperative electrocardiograph showing an incomplete right bundle branch block with evidence of right ventricular hypertrophy There is no evidence of left ventricular hypertrophy (Paper speed, 50 mm/sec)

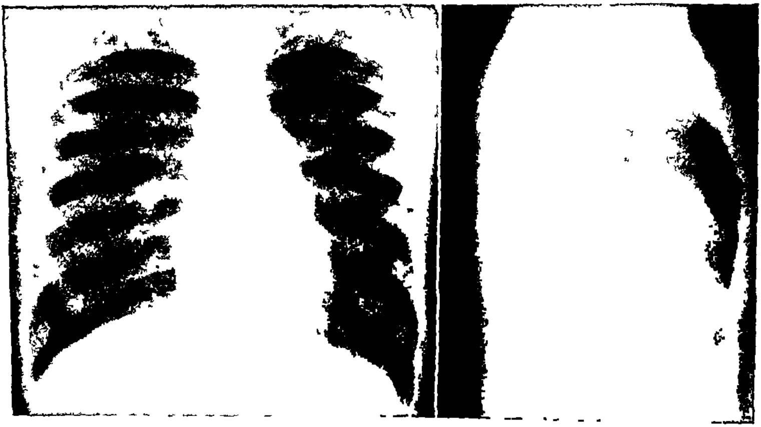

Fig 14—Case 5 PA and right la showing a normal trans
verse heart diameter with right ventricu monary conus is prominent
the right pulmonary artery is enlarged, lds are clear These are
the typical findings in individuals with s and right-to-left shunt
ing.

At the first stage operation, an abbreviated incision was first made through the right fourth intercostal space and a generous lung biopsy was obtained from the upper lobe for frozen section examination The vascular changes appeared to be only moderately severe (Fig 15), and so the operation was continued The right ventricle was markedly hypertrophied The pulmonary artery was enormous and very tense, and it was feared that an attempt at partially excluding its lumen with a clamp might tear it Therefore, the bypass was instituted and, with a partial exclusion clamp on the aorta and pulmonary artery, elliptical pieces of tissue were removed from each An aortic homograft, 12 mm in diameter, was easily and quickly anastomosed to each great vessel The aorta was then cross clamped distal to the graft site and, aided by potassium citrate arrest, a 17 mm interventricular septal de was closed with a double-thickness Teflon cloth patch. The oozing from the graft suture lines was troublesome, but after the protamine had taken effect, and with the insertion of additional sutures, good hemostasis was finally obtained. Postoperatively, the child was alert and, during the first 24 hours, he seemed to be progressing satisfactorily. A soft systolic murmur could be heard over the upper end of the sternum. Approximately 28 hours postoperatively, his

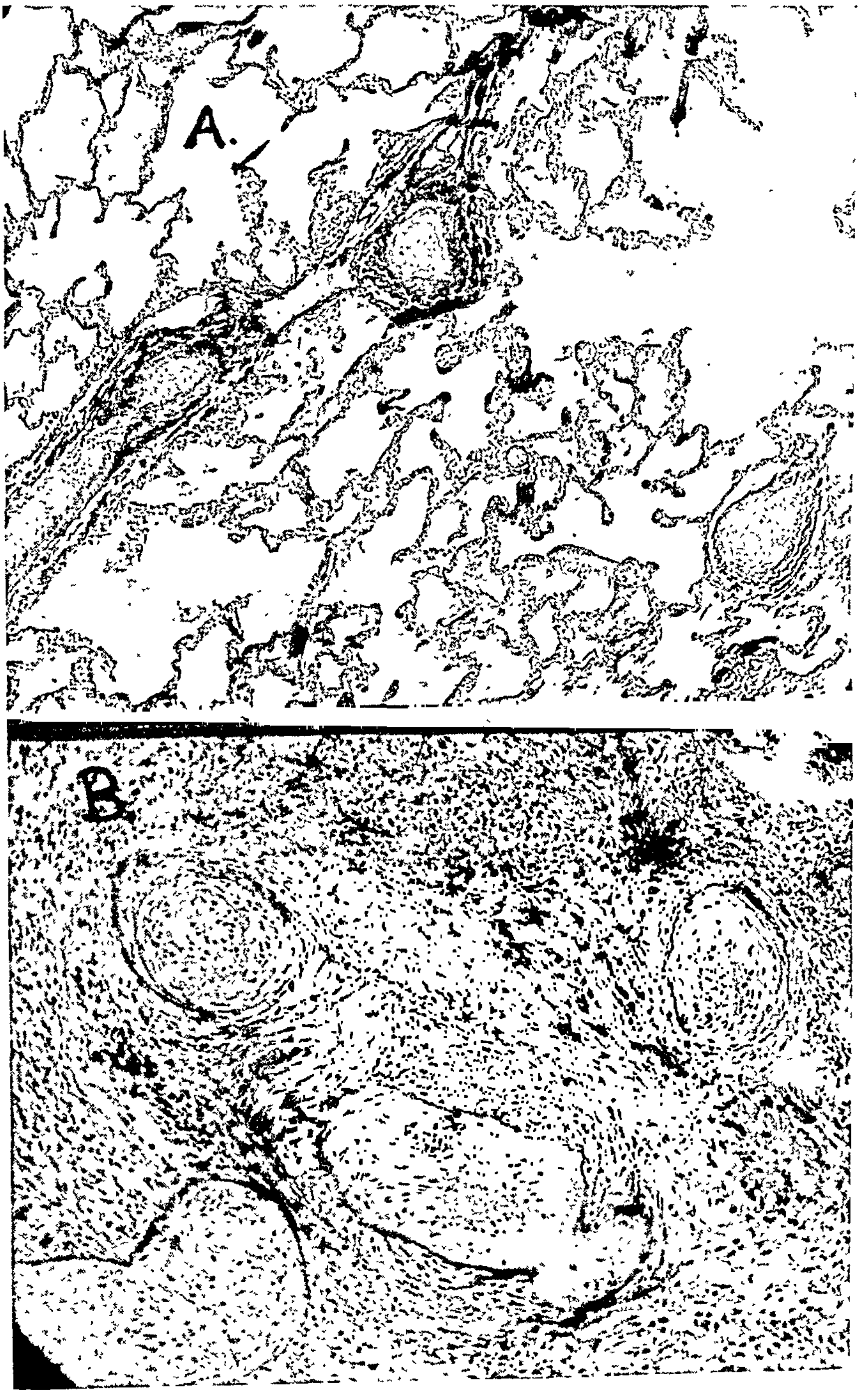

Fig. 15.—Case 5. *A*, Surgical biopsy showing dilated arteries with atrophic media compared with, *B*, tissue obtained at autopsy from a more central area of the lung. The irreversible vascular changes seen in the "Eisenmenger lung" are well demonstrated (× 100).

general condition began to deteriorate. His blood pressure dropped, and the pulse and respiration rose. The murmur could no longer be heard. His condition continued to deteriorate and he died 2 hours later.

Comment: This patient was undoubtedly of the Eisenmenger type with advanced, irreversible vascular changes and a minimal left-to right shunt. Evidence for this was the x ray appearance of a small heart, the practically normal fluoroscopic appearance of the activity of the pulmonary arteries, and a minimal step up in saturation of the right ventricular blood sample. The suggestive early desaturation of the arterial blood and the high hemoglobin value were additional corroborative evidence. He should not have been selected for the operation. Furthermore, it is probable that this patient would not have tolerated later closure of the "ductus" even if he had survived the first stage.

At autopsy, clotting of the graft was confirmed. This is not surprising in view of the very small flow which passed across it.

It was interesting to see the discrepancy between the histopathologic appearance of the lung tissue obtained by lung biopsy (Fig. 15, *A*) and that obtained at autopsy from a more central portion of the lung (Fig. 15, *B*). As Edwards[7] has pointed out, dilated and atrophic vessels may be found distal to the advanced occlusive changes found in the Eisenmenger lung. Thus, if this is not kept in mind, especially when none of the severely afflicted arteries are seen, the biopsy may be misinterpreted.

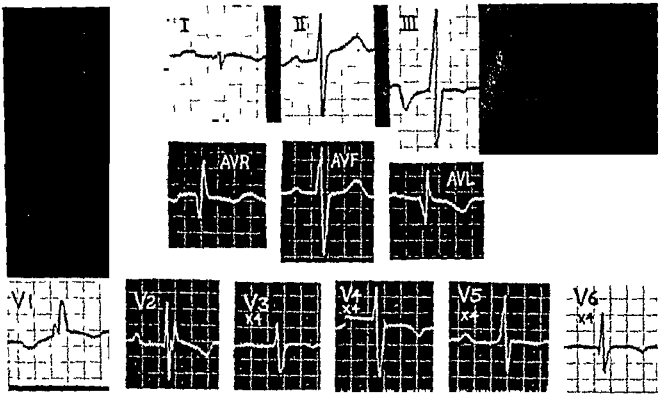

Fig. 16.—Case 6. Preoperative electrocardiogram indicates hypertrophy of both right and left ventricles. (Paper speed, 50 mm./sec.)

Case 6.—B. McC., a 5 year old girl, had been admitted to the Children's Hospital 2 years previously for the repair of a cleft palate and harelip. In addition to a heart murmur, a double kidney and hemivertebrae were found. The child suffered from repeated respiratory infections and had a decreased exercise tolerance.

She was below the third percentile in growth. There was a Grade 3 (1-4) systolic murmur present which was loudest in the fourth left intercostal space and was transmitted over the entire precordium. P_2 was accentuated.

The electrocardiograph (Fig. 16) showed both right and left ventricular hypertrophy. A teleoroentgenogram (Fig. 17) demonstrated the enlarged heart and an accentuation of the pulmonary vascularity. On fluoroscopy, the pulmonary artery activity was considered to be moderately increased—slightly more than the other similar cases in this series. Cardiac catheterization was performed (Table VI). The diagnosis was made of interventricular septal defect with equal pressure pulmonary hypertension and significant left-to right shunt. She was discharged to await readmission for the two-stage operation.

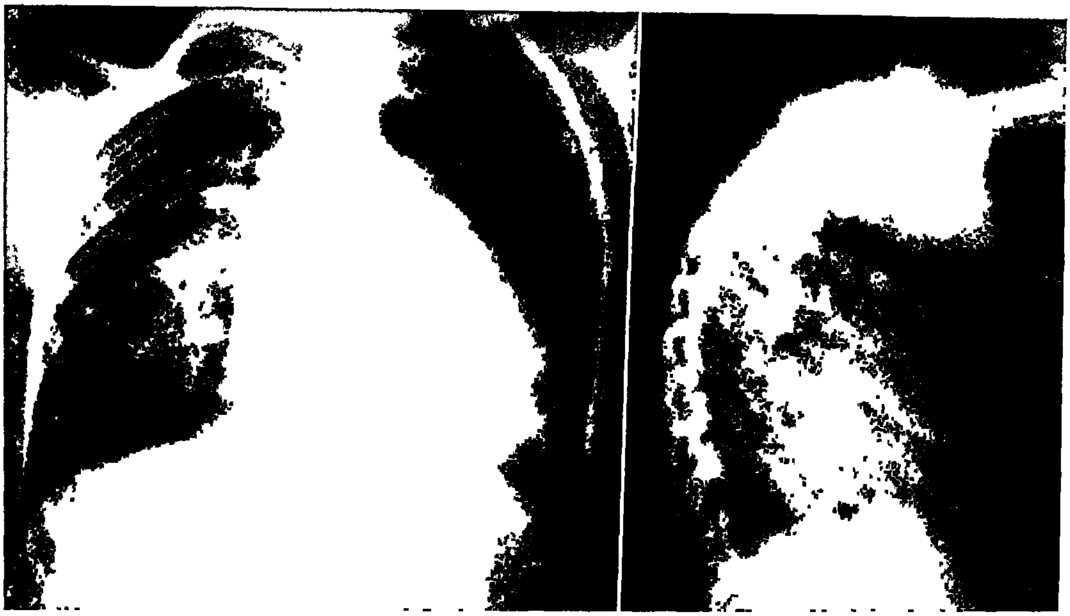

Fig 17 —Case 6 PA and right lateral chest roentgenograms showing cardiac enlargement and marked accentuation of the pulmonary vascularity

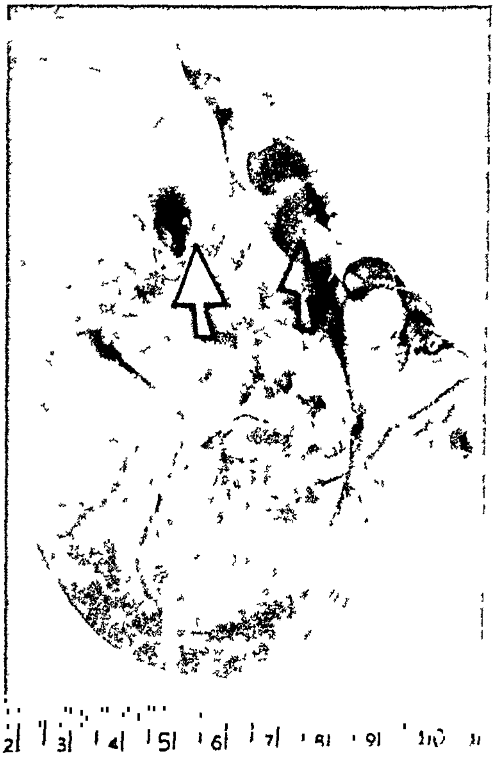

Fig 18 —Case 6 Autopsy photograph of the posterior aspect of the heart with the pulmonary artery (*left*) and aorta (*right*) opened The narrow orifices produced by the longitudinal incisions are well illustrated Both anastomotic sites are clotted

On Feb. 7, 1958, the first stage was undertaken. Because of the technical difficulties at the second stage in Case 4, a nylon graft (Edwards-Tapp), 3/8 inch inside diameter, was placed between the ascending aorta and pulmonary artery. Each time an ample segment of aorta was excluded by the clamp, a fall in blood pressure occurred. Therefore, instead of removing an elliptical piece of tissue, it was decided to resort to a longitudinal incision in the aorta. Although mindful of the previous experience in Case 2, it was thought that the

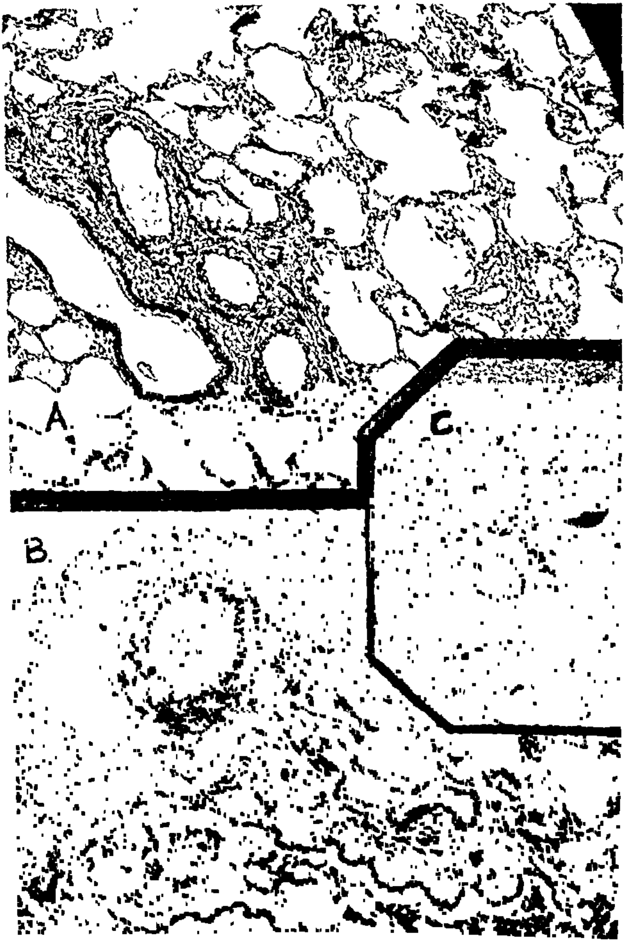

Fig. 19.—Case 6. *A*, Photomicrograph of peripheral biopsy obtained at surgery. *B* and *C*, Photomicrographs of more centrally located tissue obtained after the patient's death. The changes appear more severe than in *A*.

TABLE VI

B. MC C.	PREOPERATIVE	
	SATURATION PER CENT	PRESSURE (MM. HG)
Superior vena cava	69	
Right atrium	68	6.5
Right ventricle	85	84/0
Main pulmonary artery	89	84/36
Brachial artery	100	84/52

Case 6. Preoperative studies indicating a large shunt at the ventricular level and equal-pressure pulmonary hypertension.

large diameter of the graft would compensate for failure to remove elliptical pieces of vessel wall and assure patency at least for a sufficient time to permit recovery. The bypass was established and, employing potassium citrate arrest, a 17 mm. septal defect was closed with a Teflon cloth patch. Following perfusion, the patient's condition appeared satisfactory. She was alert, her color was good and the vital signs were stable. A loud systolic shunt murmur could be heard over the upper end of the sternum. The blood pressure was 105/55 mm. Hg, typically a wide pulse-pressure ductus type. Suddenly, 3½ hours after surgery, in a matter of seconds, her condition dramatically changed. Her skin became pale, the blood pressure became unobtainable, and the pulse and respiration rose. Coincidentally, it was noted that the shunt murmur had disappeared. It was suspected that the graft had become clotted and that this had precipitated the sudden reversal in the patient's condition. With the aid of resuscitative measures, including small amounts of blood and vasopressors, the child rallied and the blood pressure returned to 80/60 mm. Hg. However, the child continued to appear "shocky." Her color remained poor and the fast pulse and respiration persisted. The shunt murmur never returned. The child continued in this fashion for another 7½ hours and then died.

Comment: This child had the largest left-to-right shunt in the entire series as demonstrated by fluoroscopic study and the step-up in saturation of the right ventricular sample. This evidence of high flow might have led one to predict preoperatively that the child could have survived a single-stage approach. However, bedside observations made during the postoperative period established that the functioning "ductus" was necessary and that its occlusion by thrombus (Fig. 18) precipitated the sudden and fatal cardiovascular deterioration. One might take the opposite view that shock occurred suddenly causing the murmur to disappear and the other events which followed. Unfortunately, under these circumstances it is not practical to obtain suitable objective data. One must rely instead upon clinical impressions. In support of the first explanation was the suddenness with which the patient's condition changed after a satisfactory earlier postoperative response. This behavior contrasts sharply with those similar cases treated by one-stage surgery who show evidence of a failing circulation as soon as the bypass is discontinued. These early signs are readily recognized and soon produce a clinical picture similar to the one presented by this child after the graft became clotted. In our experience, their appearance presages an imminent fatal outcome.

The histologic sections showed moderately severe vascular changes. Those obtained at autopsy from the central areas (Fig. 19, *B* and *C*) of the lung appear more pronounced than those found in the tissue obtained by surgical biopsy (Fig. 19, *A*).

DISCUSSION

The initial event occurring after conventional corrective surgery that is responsible for the ultimate death of these equal-pressure pulmonary hypertensive patients has not been precisely identified. There may arise an exaggerated vasospastic component which superimposes itself on the already abnormal arterial bed. The medial hypertrophy seen on microscopic examination would suggest that the muscular arteries are indeed capable of a vigorous vasomotor reaction. Perhaps this response is precipitated by suddenly removing the excessive pulmonary blood flow or by the manipulation of the lungs. When this is added to those other burdens imposed by suddenly reversing the adapted state and by extensive surgery on the heart itself, the cardiopulmonary system may very likely be overwhelmed. Therefore, if these patients are to survive operation it would seem reasonable (1) to avoid an immediate alteration of this compensated state by achieving the desired result gradually in two stages, and (2) to plan the two stages so that the least physiologic readjustment will be required at the time of the greatest operative undertaking. This can be accomplished if, at the first stage, an ample left-to-right flow is perpetuated by using a graft of large diameter and by being careful with details of the anastomoses to assure patency. Anastomoses made to longitudinal incisions, a technique which has been used successfully in the past in other vascular procedures, have produced clotting of the "ductus" in these patients. This difference in results is probably due to the special conditions of blood flow across the graft. Even though it may have the same diameter as the septal defect, the left-to-right shunt will still be reduced by the influence of other factors governing flow in tubes, such as length and contour of the graft, the characteristics of its internal surface and the configuration of the anastomotic orifices.

The second stage is performed 3 to 6 months later, after the heart and lungs have recovered from the initial operative intervention. Thus, the more physiologically strenuous burden imposed on the cardiopulmonary system by completely abolishing the shunt will be made to coincide with an operative procedure equal to closing a patent ductus.

Because of the various combinations of plumonary flow and resistance which may interact to cause elevation of the pulmonary artery pressures to systemic levels, those patients with equal-pressure pulmonary hypertension constitute a physiologically heterogeneous group. This has been well documented by Dammann[8] and Edwards.[7] Therefore, although the term "equal-pressure" may be used for roughly categorizing a special group of individuals with pulmonary hypertension, it is an inadequate index for selecting patients for the two-stage operation. Those patients who are acceptable must still have a significant left-to-right shunt (Fig. 20). This selection is guided by the degree of increase over normal in the activity exhibited by the pulmonary arteries during fluoroscopy. The greater the role being played by the factor of flow through the lungs, the more expansile the pulmonary arteries and their branches become (in the absence of pulmonic insufficiency). However, it should be noted that this accentuation is not of the magnitude seen in patients with lesser degrees of pressure elevation. Also of help is the amount of increase (over that from the right atrium) in the saturation of the right ventricular blood sample obtained during catheterization. A value around 10 per cent is a favorable sign.

The remaining members of the equal-pressure group who have minimal left-to-right shunt-flow or persistent flow-reversal are not suitable candidates for the two-stage operation (Fig. 21). This transition from a significant left-to-right shunt seems to occur as the child approaches puberty. So far, *none* of the equal-pressure cases in this age range (or older) have been found acceptable. Histologic study of lung sections obtained from some of these patients has strengthened the impression that age is another important criterion for the proper selection of cases for the two-stage operation.

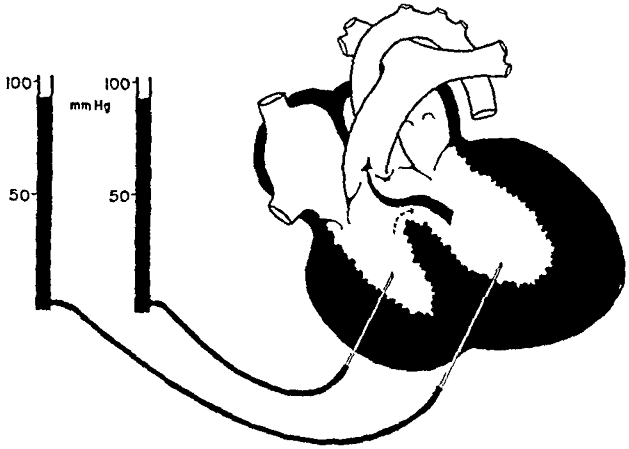

Fig. 20.—Schematic representation of the pathophysiology in an "equal-pressure" pulmonary hypertensive with residual left-to-right shunt. Here flow is still a factor in the pressure elevation. This type of patient is acceptable for the two-stage procedure.

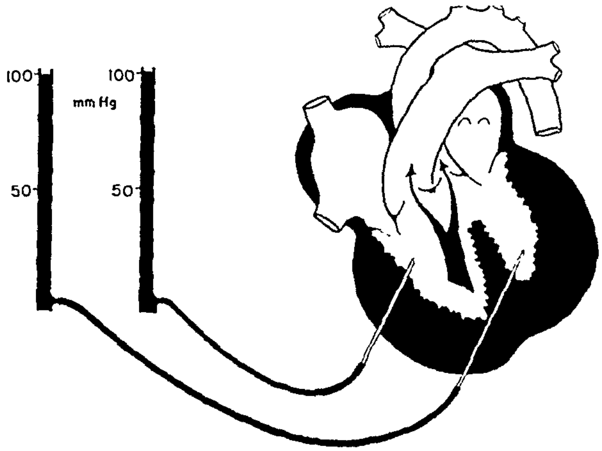

Fig. 21.—A representation of an "equal-pressure" patient in whom pulmonary resistance has exceeded systemic resistance. There is now a right-to-left shunting of blood (Eisenmenger's syndrome). This patient is not acceptable for the two-stage procedure.

SUMMARY

A two-stage operation is proposed for the surgical correction of ventricular septal defects associated with equal-pressure pulmonary hypertension. At the first stage, a large diameter graft, serving as a temporary artificial "ductus," is placed between the ascending aorta and the pulmonary artery and, with the aid of a mechanical heart-lung apparatus, the septal defect is repaired. The second stage is performed 3 to 6 months later and consists of dividing the graft, thus completing the correction of the shunt This approach is predicated on the principle of separating the burdens on the heart and lungs imposed by an operation of open heart magnitude from those imposed by suddenly reversing the patient's compensated pathophysiologic state At Stage I, the cardiovascular system is called upon to make a minor physiologic readjustment coincident with an operation of great magnitude Conversely, at Stage II, the burden is similarly minimized by using a lesser surgical procedure when the demands of physiologic compensation are likely to be most severe

The proper selection of cases depends upon choosing those patients with equal pressure with a significant left to right shunt The most helpful guides have been the activity of the pulmonary artery, as determined fluoroscopically, and the catheterization data Age is also an important factor The results so far have been encouraging in that 3 of the 5 properly selected patients have survived Follow-up catheterization studies have shown a return to normal hemodynamics

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EDITOR'S NOTE The discussion of the preceding paper (Sirak and Hosier) will be published in an upcoming issue following the paper entitled 'Corrective Surgery in the Presence of Far Advanced Pulmonary Hypertension' by Dr C Walton Lillehei and associates, with which it was discussed

SURGICAL TREATMENT FOR THE TETRALOGY OF FALLOT BY OPEN INTRACARDIAC REPAIR

John W. Kirklin, M.D., F. Henry Ellis, Jr., M.D., Dwight C. McGoon, M.D. (by invitation), James W. DuShane, M.D. (by invitation), and H. J. C. Swan, M.B., Ph.D. (by invitation), Rochester, Minn.

THE PROGRESSING invalidism usually imposed by the combination of malformations known as the "tetralogy of Fallot" has long stimulated search for effective treatment. Wide acclaim properly greeted the discovery of Blalock and Taussig[1] that an anastomosis between a systemic and pulmonary artery resulted in amelioration of cyanosis and polycythemia and improved exercise tolerance in the patient with tetralogy of Fallot. The beneficial effect of increased pulmonary blood flow was again demonstrated in the results obtained by Potts[2] utilizing anastomosis of the aorta and pulmonary artery. Brock[3] logically argued that pulmonary flow could be increased by directing the surgical endeavor toward relief of the pulmonary stenosis. He showed that good palliation could be achieved in many patients by pulmonary valvotomy and infundibular resection done by a closed technique. Many surgeons dreamed of complete repair of the tetralogy of Fallot, but it was first accomplished by Lillehei and associates in 1954 using whole body perfusion established by the technique of controlled cross-circulation.[4]

General agreement has not been reached as yet concerning the surgical technique of choice for the treatment of the tetralogy of Fallot. Experience with patients treated by open intracardiac repair at the Mayo Clinic since April, 1955, has led us to conclude that this is an effective treatment for tetralogy of Fallot. Data concerning these cases and a discussion of them form the basis for this report.

DEFINITION

Since there is a wide variation among hearts with pulmonary stenosis and ventricular septal defect, it appears unreasonable to designate them all as the tetralogy of Fallot. Apparent dextroposition of the aorta occurs in some patients with ventricular septal defect and no pulmonary stenosis and there may be no dextroposition in a few patients seeming to have otherwise typical tetralogy of Fallot. This feature does not then serve well to identify the tetralogy of Fallot. It has been suggested that the term "tetralogy of Fallot" be discarded

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From the Mayo Clinic and Mayo Foundation.

Read at the Thirty-eighth Annual Meeting of The American Association for Thoracic Surgery, Boston, Mass., May 16-18, 1958.

in recognition of the fact that this condition shades off toward severe pulmonary stenosis with a very small ventricular septal defect or toward a large ventricular septal defect with mild pulmonary stenosis.

Clinically and surgically, the term continues to have sufficient usefulness to justify its retention. For this study, tetralogy of Fallot is defined as a congenital cardiac malformation with ventricular septal defect of a size approximating the aortic orifice and pulmonary stenosis of such severity that it, in combination with the ventricular septal defect, results in identical right and left ventricular pressures. There are varying degrees of dextroposition, or overriding of the aorta, in specimens meeting these criteria. The pulmonary stenosis is usually infundibular, either isolated or in combination with stenosis of the pulmonary valve.[5, 6] Rarely, the stenosis is limited to the pulmonary valve.

In most patients with tetralogy of Fallot, high resistance to right ventricular emptying is posed by the pulmonary stenosis, the direction of the shunt across the ventricular septal defect is right to left and, as a result, cyanosis is present. When the resistance posed by the pulmonary stenosis is less severe, the shunt may be bidirectional. Uncommonly, the resistance posed by the stenosis is sufficiently low that only a left-to-right shunt occurs, although pressures in the two ventricles are identical. Since some patients who were acyanotic early in life are cyanosed in later childhood, it is assumed that the relative severity of the pulmonary stenosis can increase.

MATERIAL AND METHODS

All patients except one with the tetralogy of Fallot undergoing operation on one surgical service at the Mayo Clinic since April 1, 1955, were treated by open intracardiac repair. For the one exception, a severely handicapped woman 28 years old, operated on in the summer of 1955, the Brock infundibular resection was done. All the patients treated on this service by open intracardiac repair until May 1, 1958, are included in this report.

Data concerning all patients treated by open intracardiac repair on this service in this period are given in Table I. Remarks concerning disability and cyanosis are based on the history and physical examination. Associated defects and previous operations are noted there. The anatomy of the pulmonary stenosis given in the table was determined at operation. When the pulmonary artery was so narrow that it seemed to offer significant resistance to right ventricular emptying, it is listed as an obstructing lesion.

Data concerning patients surviving operation and hospitalization are shown in Table II. The present status and cyanosis given in this table are those determined by history and examination. A clinical evaluation was made of the repair of the ventricular septal defect on the basis of the auscultation and roentgenography of the thorax at postoperative examinations. The possible limitations of this type of evaluation are recognized. It is doubtful, however, that large residual shunts can be present without clinical manifestations. Postoperative catheterization data when available were used. Evaluation of the

TABLE I. OPEN INTRACARDIAC REPAIR

CASE†	AGE, YEAR	SEVERITY OF DISABILITY	CYANOSIS		ARTERIAL O_2 SATURATION (PER CENT)		ADDITIONAL DEFECTS OR PREVIOUS OPERATION	SITE OF PULM NARY STENOS	
			REST	EXERCISE	REST	EXERCISE‡		INFUNDIBULUM	VALVE§
1	5	Sev.	Mod.	Sev.			Left subclavian A. to PA anastomosis (1951)	+	–
2	4	Sev.	Sev.	Sev.	70	44		+	+
3	7	Sev.	Mild	Mod.				+	–
4	17	Mod.	None	Mod.				+	+
5	3	Sev.	Mild	Mod.	92	86		+	+
6	8	Mod.	Mild	Mod.	89	83		+	+
7	11	Sev.	None	Mild				+	+
8	5	Mod.	Mild	Sev.	84	61	Agenesis of Left PA	–	+
9	6	Sev.	Mod.	Sev.	86	67		+	+
10	7	Sev.	Sev.	Sev.				+	+
11	28	Mod.	None	None	95			+	–
12	2	Mod.	Mod.	Sev.	78	61		+	+
13	5	Sev.	Mod.	Sev.	81	56		+	–
14	13	Sev.	Mod.	Sev.	80	49	Left subclavian A. to PA anastomosis (1948)	+	–
15	3	Mod.	Mod.	Sev.	82	75		+	+
16	17	Mod.	None	Mod.	97	69		+	+

TETRALOGY OF FALLOT: ALL 74 CASES*

METHOD OF REPAIR				PRESSURES MEASURED IN OPERATING ROOM AFTER REPAIR, MM. HG			HOSPITAL FATE	PROBABLE CAUSE OF DEATH
	PULMONARY STENOSIS							
VSD§	RESECTION AND/OR VALVOTOMY	OUTFLOW TRACT (IVALON)	COMPLETE IVALON RECONSTRUCTION‖	PA	RV	AORTA		
	+	−	−				Died 2 hr. p.o. with pulm edema	Perfusion; VSD repair complete at necropsy
Ivalon (early method)	+	−	−				Died 10 hr p.o. with pulm edema	Related to perfusion and incomplete repair of VSD
Ivalon (early method)	+	−	−				Died at end of operation	Heart block
	+	−	−				Died 8 hr. p.o.	Hemorrhage, related to perfusion
Ivalon (early method)	+	−	−				Died 4 hr. p.o.	Perfusion; incomplete relief of pulmonary stenosis
Ivalon (early method)	+	−	−				Survived	
Ivalon (early method)	+	−	−				Survived	
Ivalon (early method)	+	−	−				Survived	
Ivalon (early method)	+	−	−	34/15	$\frac{100}{10\ 18}$	86/53 (radial)	Survived	
Ivalon (early method)	+	−	−		124/18	38/29	Died at end of operation	Incomplete relief of pulmonary stenosis
Ivalon (early method)	+	−	−	23/8	45/0	64/35	Survived	
Ivalon (early method)	+	−	−				Died 12 hr. p.o.	Heart block; incomplete repair of VSD, probably incomplete relief of pulmonary stenosis
Ivalon (early method)	+	−	−				Survived	
Ivalon (early method)	+	−	−	32/7	52/5	77/85	Died 12 hr p.o.	Incomplete repair VSD
Direct suture	+	+	−	24/12	53/7	81/58	Survived	
Ivalon (early method)	+	+	−	19/8	22/4	70/30	Survived	

TABLE I. OPEN INTRACARDIAC REPAIR

ASE†	AGE, YEAR	SEVERITY OF DISABILITY	CYANOSIS		ARTERIAL O_2 SATURATION (PER CENT)		ADDITIONAL DEFECTS OR PREVIOUS OPERATION	SITE OF PULM NARY STENOS	
			REST	EXERCISE	REST	EXERCISE‡		INFUNDIBULUM	VALVE§
1	5	Sev.	Mod.	Sev.			Left subclavian A. to PA anastomosis (1951)	+	−
2	4	Sev.	Sev.	Sev.	70	44		+	+
3	7	Sev.	Mild	Mod.				+	−
4	17	Mod.	None	Mod.				+	+
5	3	Sev.	Mild	Mod.	92	86		+	+
6	8	Mod.	Mild	Mod.	89	83		+	+
7	11	Sev.	None	Mild				+	+
8	5	Mod.	Mild	Sev.	84	61	Agenesis of Left PA	−	+
9	6	Sev.	Mod.	Sev.	86	67		+	+
10	7	Sev.	Sev.	Sev.				+	+
11	28	Mod.	None	None	95			+	−
12	2	Mod.	Mod.	Sev.	78	61		+	+
13	5	Sev.	Mod.	Sev.	81	56		+	−
14	13	Sev.	Mod.	Sev.	80	49	Left subclavian A. to PA anastomosis (1948)	+	−
15	3	Mod.	Mod.	Sev.	82	75		+	+
16	17	Mod.	None	Mod.	97	69		+	+

TETRALOGY OF FALLOT: ALL 74 CASES*

METHOD OF REPAIR				PRESSURES MEASURED IN OPERATING ROOM AFTER REPAIR, MM. HG				
	PULMONARY STENOSIS							
VSD§	RESECTION AND/OR VALVOTOMY	OUTFLOW TRACT (IVALON)	COMPLETE IVALON RECONSTRUCTION‖	PA	RV	AORTA	*HOSPITAL FATE*	*PROBABLE CAUSE OF DEATH*
	+	–	–				Died 2 hr. p o with pulm edema	Perfusion; VSD repair complete at necropsy
Ivalon (early method)	+	–	–				Died 10 hr. p o with pulm edema	Related to perfusion and incomplete repair of VSD
Ivalon (early method)	+	–	–				Died at end of operation	Heart block
	+	–	–				Died 8 hr. p o.	Hemorrhage, related to perfusion
Ivalon (early method)	+	–	–				Died 4 hr. p o.	Perfusion; incomplete relief of pulmonary stenosis
Ivalon (early method)	+	–	–				Survived	
Ivalon (early method)	+	–	–				Survived	
Ivalon (*early* method)	+	–	–				Survived	
Ivalon (early method)	+	–	–	34/15	$\frac{100}{10\ 18}$	86/53 (radial)	Survived	
Ivalon (early method)	+	–	–		124/18	38/29	Died at end of operation	Incomplete relief of pulmonary stenosis
Ivalon (early method)	+	–	–	23/8	45/0	64/35	Survived	
Ivalon (early method)	+	–	–				Died 12 hr. p o	Heart block; incomplete repair of VSD, probably *incomplete relief* of pulmonary stenosis
Ivalon (early method)	+	–	–				Survived	
Ivalon (early method)	+	–	–	32/7	52/5	77/85	Died 12 hr. p o	Incomplete repair VSD
Direct suture	+	+	–	24/12	53/7	81/58	Survived	
Ivalon (early method)	+	+	–	19/8	22/4	70/30	Survived	

TABLE I

CASE†	AGE, YEAR	SEVERITY OF DISABILITY	CYANOSIS		ARTERIAL O_2 SATURATION (PER CENT)		ADDITIONAL DEFECTS OR PREVIOUS OPERATION	SITE OF PULMONARY STENOSIS		
			REST	EXERCISE	REST	EXERCISE‡		INFUNDIBULUM	VALVE§	PA
17	7	Mod.	None	Mild	95	87		+	–	–
18	9	Sev.	Mild	Sev.	87	65	Atrial septal defect	+	+	+
19	11	Mod.	None	None				+	–	–
20	9	Mild	None	None	97			+	–	–
21	14	Sev.	Mild	Sev.	92	61		+	–	–
22	15	Sev.	Mild	Mod.	90	79		+	–	–
23	6	Mild	None	None				+	+	–
24	3	Sev.	Mod.	Sev.	79	49		+	–	+
25	6	Sev.	Mod.	Sev.	80	44	Patent ductus arteriosus from which originated left subclavian A.	+	–	–
26	4	Sev.	None	Mod.				+	+	–
27	19	Mod.	None	Slight	95	93		+	+	–
28	7	Sev.	Mod.	Sev.	72	58		+	–	–
29	8	Mod.	Mild	Mod.	90	51		+	+	–
30	6	Sev.	Mild	Mod.	93	85	Left subclavian to PA anastomosis (1953)	+	+	+
31	9	Sev.	Mild	Mod.	82		Persistent left superior vena cava	+	+	–
32	1⅚	Sev.	Mod.	Sev.	66	50	Agenesis left coronary A. with anomalous right coronary A.	+	+	+
33	24	Sev.	None	None	95			+	+	–

(CONT'D)

METHOD OF REPAIR				PRESSURES MEASURED IN OPERATING ROOM AFTER REPAIR, MM. HG				
	PULMONARY STENOSIS							
VSD§	RESECTION AND/OR VALVOTOMY	OUTFLOW TRACT (IVALON)	COMPLETE IVALON RECONSTRUCTION‖	PA	RV	AORTA	HOSPITAL FATE	PROBABLE CAUSE OF DEATH
Ivalon (early method)	+	–	–	18/2	23/1	105/56	Survived	
Ivalon (early method)	+	+	+	24/6	45/0	70/35	Survived	
Ivalon (early method)	+	–	–	37/15	42/10	95/32	Survived, temporary heart block	
Ivalon (early method)	+	–	–	20/7	24/0	95/50	Died 12 hr. p.o. of progressive hypertension	Cardiac tamponade
Ivalon	+	–	–				Survived	
Ivalon	+	–	–	36/9	44/0	106/60	Survived	
Ivalon	+	–	–	17/10	20/0	75/44	Survived	
Ivalon	+	+	–	32/15	57/0	85/57	Died 14 hr p.o.	In part, perfusion (probable hypovolemia); in part, incomplete relief of pulmonary stenosis
Ivalon	+	+	–	38/17	43/8	85/52	Died 3 hr. p.o.	Artifically created systemic hypertension
Direct suture	+	–	–		35/4	98/42	Survived	
Ivalon	+	–	–	15/2	40/5	78/46	Survived, temporary heart block	
Direct suture	+	–	–	35/12	51/11	62/27	Died 7 hr. p.o.	Poor perfusion, surgery therefore done in haste and poorly, heart block, incomplete relief of pulmonary stenosis
Ivalon	+	–	–	25/10	42/0	65/37	Survived	
Ivalon	+	+	–	27/5	35/2	75/40	Survived	
Direct suture	+	–	–	27/7	30/0	85/50	Survived	
Ivalon	+	+	+	16/4	35/0	57/20	Died at end of operation	Division of single coronary artery
Ivalon	+	–	–	16/10	32/4	95/60	Survived	

TABLE I

CASE†	AGE, YEAR	SEVERITY OF DISABILITY	CYANOSIS		ARTERIAL O_2 SATURATION (PER CENT)		ADDITIONAL DEFECTS OR PREVIOUS OPERATION	SITE OF PULMONARY STENOSIS		
			REST	EXERCISE	REST	EXERCISE‡		INFUNDIBULUM	VALVE§	PA
34	9	Mod.	Mod.	Mod.	82	81		+	+	+
35	31	Sev.	Mod.	Sev.	65	40		+	+	−
36	5	Mod.	Mild	Mod.			Diabetes mellitus	+	+	−
37	1¼	Sev.	Mild	Sev.	86	69		+	+	−
38	5	Mod.	None	Mod.	91	79	Persistent left superior vena cava	+	+	−
39	35	Mod.	None	Mild	96		Small persistent left superior vena cava	+	+	−
40	5	Mild	None	None	97			+	−	−
41	8	Sev.	None	Sev.	95	64		+	+	+
42	6	Sev.	Sev.	Sev.	78	57	Potts' anastomosis (1953) and previous Brock operation (1954)	+	−	−
43	3	Sev.	Mod.	Sev.				+	+	+
44	13	Sev.	Mild	Mod.	91	73	ASD; anomalous right coronary A.	+	−	−
45	17	Sev.	Sev.	Sev.			None	+	+	−
46	8/12	Sev.	Mod.	Mod.	87	78		+	+	−
47	21	Sev.	Mod.	Sev.				+	+	−
48	7	Mod.	None	Mod.	95	80		+	−	−
49	7	Sev.	Mild	Mod.	95	61	Large azygos and hemiazygos veins; small IVC	+	+	−
50	20	Sev.	Mod.	Sev.	81	61		+	−	−
51	10	Mod.	Mild	Mod.	94	85	Small patent ductus arteriosus	+	+	−
52	11	Mod.	Mod.	Sev.	80		Anomalous right coronary A. supplying left ant. desc. coronary A. (preserved)	+	−	−
53	2½	Sev.	Mod.	Mod.	84	73		+	+	+
54	7	Sev.	Sev.	Sev.	68	43		+	+	−

(CONT'D)

	METHOD OF REPAIR							
	PULMONARY STENOSIS			PRESSURES MEASURED IN OPERATING ROOM AFTER REPAIR, MM. HG				
VSD§	RESECTION AND/OR VALVOTOMY	OUTFLOW TRACT (IVALON)	COMPLETE IVALON RECONSTRUCTION‖	PA	RV	AORTA	HOSPITAL FATE	PROBABLE CAUSE OF DEATH
Direct suture	+	−	−		80/5	80/50	Survived	
Ivalon	+	+	−	35/15	37/2	85/44	Died 24 days p.o.	Pseudomonas endocarditis and bacteremia
Direct suture	+	−	−	40/27	80/27	68/25	Died 12 hr p.o.	Inadequate relief of pulmonary stenosis
Direct suture	+	−	−				Survived	
Direct suture	+	+	−		55/10	100/55	Survived	
Ivalon	+	−	−	25/16	40/11	81/51	Survived	
Direct suture	+	−	−	21/6	25/4	75/44	Survived	
Ivalon	+	+	+	24/14	61/9	108/62	Survived	
Ivalon	+	+	−		34/4	92/47	Survived	
Ivalon	+	+	+	20/10	37/6	75/42	Survived	
Ivalon	+	−	−	18/7	36/6	115/91	Died 48 hr p.o.	Division of anomalous right coronary A. supplying left anterior desc. coronary A.
Ivalon	+	+	+	34/8	47/5	90/48	Survived	
Direct suture	+	+	−		52/10	71/40	Died 3 hr p.o.	Perfusion
Ivalon	+	+	−	27/17	48/9	65/40	Survived	
Direct suture	+	−	−	23/10	27/4	79/44	Survived	
Direct suture	+	+	+	23/11	53/3	100/60	Survived	
Direct suture	+	−	−	29/14	38/26	99/61	Survived	
Direct suture	+	−	−	25/11	37/7	104/54	Survived	
Ivalon	+	−	−	34/9	38/4	108/62	Survived	
Direct suture	+	+	+				Survived	
Direct suture	+	−	−	32/12	65/11	[illegible]	[illegible]	[illegible]

TABLE I.

CASE†	AGE, YEAR	SEVERITY OF DISABILITY	CYANOSIS		ARTERIAL O_2 SATURATION (PER CENT)		ADDITIONAL DEFECTS OR PREVIOUS OPERATION	SITE OF PULMONARY STENOSIS		
			REST	EXERCISE	REST	EXERCISE‡		INFUNDIBULUM	VALVE§	PA
55	12	Mild	None	None	97	95		+	–	–
56	4	Sev.	Sev.	Sev.	65		Anomalous right coronary A. supplying left ant. desc. coronary A. (preserved)	+	+	+
57	27	Mod.	Mod.	Mod.				+	+	–
58	9	Sev.	Mod.	Sev.	83	60		+	+	+
59	3	Sev.	Mod.	Sev.	83	78		+	+	+
60	5	Sev.	Mod.	Sev.	74	37		+	–	–
61	16	Sev.	Mild	Mod.				+	–	–
62	$1\frac{5}{6}$	Sev.	Mild	Sev.	85	53		+	+	+
63	23	Mod.	Mild	Mod.	92	86		+	+	+
64	3	Sev.	Mild	Mod.	89	81	ASD	+	+	–
65	5	Mod.	Mod.	Mod.	84	73		+	+	–
66	3	Mod.	Mod.	Sev.	78	68		+	+	+
67	6	Mod.	Mild	Mod.	89	81	ASD	+	+	–
68	4	Mod.	Mild	Mod.	92	85	ASD	+	+	–
69	5	Sev.	Mod.	Mod.	87	76	Small patent ductus arteriosus	+	+	+
70	5	Mod.	Mild	Mild				+	+	–
71	17	Mod.	Mild	Mod.	89		Situs inversus	+	+	–
72	6	Mod.	Mod.	Sev.	70	58		+	–	–
73	10	Sev.	Mod.	Mod.	85	71	Associated ASD; left subclavian to PA anastomosis (1950); brain abscess (1956)	+	+	–
74	29	Mod.	Mild	Mod.			Left subclavian to PA anastomosis (1956)	+	+	–

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*Abbreviations used in this table and in Table II are: PA = pulmonary artery; VSD = ventricular septal defect; RV = right ventricle; A. = artery; AV = atrioventricular; IVC = inferior vena cava; ASD = atrial septal defect; Sev. = severe; Mod. = moderate.

†In a previous article,[7] deaths due to perfusion were analyzed. Cases in which death occurred considered in that article and also in this one are Cases 1, 2, 3, 4, 5, 9, 12, 14, 20, 24, 25, 28, 32, 35, 36, 44, and 46. In the previous article the cases were listed as Cases 6, 9, 10, 15, 16, 47, 63, 86, 103, 117, 125, 134, 158, 161, 165, 202 and 205, respectively.

(CONT'D)

METHOD OF REPAIR								
	PULMONARY STENOSIS			PRESSURES MEASURED IN OPERATING ROOM AFTER REPAIR, MM. Hg				
VSD§	RESECTION AND/OR VALVOTOMY	OUTFLOW TRACT (IVALON)	COMPLETE IVALON RECONSTRUCTION‖	PA	RV	AORTA	HOSPITAL FATE	PROBABLE CAUSE OF DEATH
Direct suture	+	–	–	32/15	35/7	105/60	Survived	
Ivalon	+	–	–	34/15	54/7	86/41	Died 7 hr. p.o.	Probable myocardial failure (present preoperatively) possibly long (45 min.) asystole; necropsy showed complete repair
Ivalon	+	–	–	25/10	36/10	98/58	Survived	
Ivalon	+	+	+	28/14	48/10	91/57	Died 5 hr. p.o.	Uncertain. Myocardial failure (?); asystole 46 min. (?)
Direct suture	+	+	+	28/5	41/6	112/68	Survived	
Ivalon	+	+	–	30/10	34/0-4	82/47	Survived	
Direct suture	+	–	–	19/12	25/6	74/48	Survived	
Direct suture	+	+	+	26/10	42/5	90/55	Survived	
	+	+	+				Survived	
Direct suture	+	+	+	28/11	36/9	86/34	Died 13 days p.o.	Probably chronic heart failure to which AV dissociation contributed
Ivalon	+	+	–	27/12	49/9	105/73	Survived	
Ivalon	+	+	+	23/10	56/7	86/55	Survived	
Ivalon	+	+	–	13/7	28/8	73/4	Survived	
Ivalon	+	+	–	20/10	32/8	99/53	Survived	
Ivalon	+	+	–	44/9	73/5	86/39	Survived; permanent but asymptomatic heart block	
Direct suture	+	+	–	28/6	45/5	85/47	Survived	
Ivalon	+	+	–	22/5	34/5	75/48	Survived	
Direct suture	+	–	–	21/8	44/5		Survived	
Direct suture	+	+	–	25/11	36/10	95/47	Survived; temporary heart block	
Direct suture	+	–	–	18/7	56/4		Survived	

‡Mild exercise on a treadmill for 5 min. at about 1½ miles per hour.

§Induced cardiac asystole employed first in Case 21 and routinely thereafter.

‖Complete Ivalon reconstruction indicates that the cardiotomy incision was carried across the pulmonary valve ring and onto the pulmonary artery and a prosthesis was placed in this area as well as in outflow tract of right ventricle.

TABLE II. FOLLOW-UP DATA ON PATIENTS

CASE	MONTHS BETWEEN OPERATION AND LAST EXAMINATION	STATUS AT LAST EXAMINATION					CLINICAL EVALUATION OF REPAIR	
		SYMPTOMS	CYANOSIS		ARTERIAL O_2 SATURATION (%)		VSD	PULMONARY STENOSIS
			REST	EXERCISE	REST	EXERCISE*		
6	29	Asymptomatic; full activity	None	None			Probable moderate L-to-R shunt	Fair
7	24	Asymptomatic; full activity	None	None			Complete	Good
8	16	Asymptomatic; full activity	None	None	95	95	Complete	Good
9	24	Asymptomatic; full activity	None	None	99		Complete	Good
11	7	Asymptomatic; full activity	None	None			Complete	Good
13	18	Asymptomatic; full activity	None	None	98	95	Complete	Good
15	10	Asymptomatic; full activity	None	None			Possible small L-to-R shunt	Fair
16	22	Asymptomatic; full activity	None	None	97	94	Probable small L-to-R shunt	Complete
17	11	Asymptomatic; full activity	None	None	98†	94†	Complete	Good
18	21	Asymptomatic; full activity	None	None	97	95	Complete	*Good*
19	14	Asymptomatic; full activity	None	None			Probable small L-to-R shunt	Complete
21	2	Died at home	P.O. dye-dilution curve indicated *incomplete* repair of VSD with moderate L-to-R *shunt; progressive cardiac enlargement occurred,* with ultimate death; cause of death presumed to be cardiac failure from incomplete repair of VSD					
22	11	Asymptomatic; full activity	None	None	95	93	Complete	Complete
23	10	Asymptomatic; full activity	None	None			Complete	Complete
26	18	Asymptomatic; full activity	None	None	95	94	Complete	Complete
27	10	Occasional dizzy spells; otherwise asymptomatic	None	None			Complete	Good
29	14	Asymptomatic; full activity	None	None			Complete	Complete
30	9	Asymptomatic; full activity	None	None	96	97	Complete	Good
31	15	Asymptomatic; full activity	None	None			Complete	Complete
33		Died of Pseudomonas bacterial endocarditis						
34	2	Died of chronic intractable right heart failure which seemed to result from inadequate relief of pulmonary stenosis						

37	10	Asymptomatic; full activity	None	None			Complete	Good
38	8	Had been asymptomatic and in full activity when he died after a 6-hour illness characterized by cough and respiratory distress; no necropsy					
39	18	Asymptomatic; full activity	None	None			Small L-to-R shunt	Good
40	11	Asymptomatic; full activity	None	None			Complete	Complete
41	8	Asymptomatic; full activity	None	None	96	97	Complete	Good
42	5	Asymptomatic; full activity	None	None	95	97	Complete	Complete
43	10	Asymptomatic; full activity	None	None			Complete	Good
45	10	Asymptomatic; full activity	None	None	96†	93†	Complete	Good
47	10	Asymptomatic; full activity	None	None	98	95	Complete	Good
48	10	Asymptomatic; full activity	None	None	93†	92†	Complete	Complete
49	5	Asymptomatic; full activity	None	None	99†	97†	Complete	Fair
50	7	Asymptomatic; full activity	None	None	98	96	Complete	Complete
51	7	Asymptomatic; full activity	None	None			Complete	Good
52	6	Asymptomatic; full activity	None	None	96†	91†	Complete	Complete
53	6	Asymptomatic; full activity	None	None	92†	92†	Complete	Fair
55	3	Asymptomatic; full activity	None	None			Complete	Complete
57	5	Asymptomatic; full activity	None	None	96†	94†	Complete	Complete
59	3	Asymptomatic; full activity	None	None	96†	98†	Complete	Good
60	3	Asymptomatic; full activity	None	None	98†	98†	Complete	Complete
61	3	Asymptomatic; full activity	None	None	97†	93†	Complete	Complete
62	3	Asymptomatic; full activity	None	None	96†	97†	Complete	Complete
63		‡	None	‡			Complete	Good
65		‡	None	‡	97†	95†	Complete	Good
66		‡	None	‡	95	96	Complete	Fair
67		‡	None	‡			Complete	Good
68		‡	None	‡			Complete	Good
69		‡	None	‡			Incomplete	Poor
70		‡	None	‡	96†	96†	Complete	Good
71		‡	None	‡	96†	91†	Complete	Good
72		‡	None	‡			Complete	Good
73		‡	None	‡			Complete	Good
74		‡	None	‡			Complete	Good

*Mild exercise on a treadmill for 5 minutes at 1½ miles per hour.

†Indicates arterial oxygen studies were done 2 weeks after surgery.

‡Too recent to evaluate.

effectiveness of the operation for the pulmonary stenosis was made from review of the surgical records and pressures taken at operation and from data obtained at postoperative cardiac catheterization (Table III) when this was done. The arterial oxygen saturation studies given in Table II are those made at the end of the follow-up period unless otherwise indicated. Eleven patients (Cases 63 through 74) were operated on too recently to permit evaluation of the symptomatic status and cyanosis on exercise.

TABLE III. POSTOPERATIVE CARDIAC CATHETERIZATION STUDIES IN 7 CASES

CASE	INTERVAL SINCE OPERATION (MO.)	PRESSURE, MM. Hg				SHUNT
		POSTOPERATIVE CARDIAC CATHETERIZATION			FEMORAL ARTERY	
		PA	INFUNDIBULAR RV	RV, LOW		
7	6 (e.w.)*	27/4		46/2-4	Normal by cuff	None
9	8 (e.w.)*	19/6		48/5	Normal by cuff	None
39	6	26/11	48/8	51/0-6	115/58	25% L-R
41	8	35/0	45/6	50/0	105/80	None
45	9	35/10	45/0	45/0	110/70	None
47	3	30/14	54/6-12	54/6-12	120/82	None
50	2 wk.	17/7	27/3	33/2	115/70	None

*Catheterization studies done elsewhere.

At all operations, extracorporeal circulation of blood through a modified Gibbon-type pump-oxygenator was employed.[8, 9] The surgical technique used for establishing whole body perfusion has been previously described.[10] The technique of perfusion itself has undergone some changes during the 3 years that these operations were done; since February, 1957, the perfusions have been managed in a relatively standard fashion,[11] employing flow rates of approximately 2.4 L. per minute per square meter of body surface for most patients. Cardiac asystole, induced by the Melrose technique,[12] has been routinely used since August, 1956, beginning with Case 21. The early surgical technique for closure of the ventricular septal defect before the use of asystole has been detailed.[13] Since asystole has been used, the technique basically is the same as that for isolated ventricular septal defect.[14] Prior to Case 15, pulmonary stenosis was treated by pulmonary valvotomy and by infundibular resection of varying degrees of completeness. The use of polyvinyl (Ivalon) sponge in the outflow tract and pulmonary artery[15] was then begun and, in general, the indication for its use in a given case has been that, in the judgment of the surgeon, complete valvotomy and infundibular resection alone would not provide a large enough pathway from right ventricle to pulmonary artery.

Preoperative and postoperative studies of arterial oxygen saturation at rest and during exercise were made for most patients with an ear oximeter. Postoperative cardiac catheterization was done in certain instances. In most patients, measurement and recording of intracardiac pressures were done in the operating room following repair of the defects. Necropsy was performed on all patients dying in the hospital, except one.

HOSPITAL MORTALITY AND FACTORS AFFECTING IT

Mortality.—Twenty-one of the 74 patients operated on died in the hospital, an over-all mortality rate of 28 per cent. The first 5 patients all died, and no further open operations were performed for the tetralogy of Fallot in our institution until the fall of 1955 when use of the procedure was resumed. The hospital mortality in the subsequent 69 cases was 23 per cent. In the last 25 cases there have been 4 deaths, a mortality of 16 per cent. This is probably representative of the present risk, although there have been no deaths in the last 10 cases.

Identification of the cause of death following any operation may be difficult, particularly one as complex as the open repair of tetralogy of Fallot. Table I gives the "probable cause" of death, and some comment of these and other factors related to hospital mortality seems warranted.

Perfusion.—Detailed information concerning the cases in which it was felt perfusion played a role in the fatality is given in a previous article analyzing all deaths related to perfusion.[7]

Degree of Relief of Pulmonary Stenosis as Related to Mortality.—Recordings were made in the operating room of low right ventricular and aortic pressure following repair in 58 of the 74 cases (Table I). Prior to repair in the tetralogy of Fallot, low right ventricular and left ventricular or aortic pressure are identical and pulmonary artery pressure is low. In most cases, pulmonary artery pressure was normal or slightly low after repair, the highest systolic pressure being 44, with a diastolic of 9 mm. Hg (Case 69). When pressure in the inflow portion of the right ventricle was elevated after operation, it resulted from residual pulmonary stenosis. Exact evaluation of the degree of stenosis requires data on flow at the time pressure recordings are made and these are not available in this study.

It seemed helpful to the evaluation of the degree of residual stenosis to plot systolic pressure from low in the right ventricle against that in the aorta (Fig. 1).

In 32 patients, the ratio of low right ventricular systolic pressure to aortic systolic pressure was less than 0.5. It is believed that this ratio is indicative of satisfactory relief of pulmonary stenosis. The hospital mortality was 9 per cent in this group. The ratio was 0.5 or more in 26 patients with a hospital mortality of 38 per cent. This latter group represents surgical failures, not a type of pulmonary stenosis which is inherently uncorrectable.

It is known on the basis of this experience that good relief of pulmonary stenosis can be achieved in about a third of the cases by radical resection of the crista supraventricularis, either alone or with valvotomy, and that in about a third only the *proper* employment of polyvinyl (Ivalon) sponge for enlargement of the outflow tract will suffice. Individual examples of failure and success by these various methods are shown in Figs. 2, 3 and 4. Even the difficult condition with a long, narrow outflow tract, a narrow pulmonary valve ring, and a narrow pulmonary artery can be successfully treated by proper application of Ivalon reconstruction (Fig. 5). This anatomy and thus the need for complete reconstruction are found in the remaining third of the cases.

It is believed that in 7 of the 21 deaths in this series, failure to relieve adequately the pulmonary stenosis was a significant factor in the failure to survive. One additional patient (Case 34) died 6 weeks after returning home from intractable right heart failure which probably resulted from poor relief of the pulmonary stenosis.

Completeness of Repair of Ventricular Septal Defect as Related to Mortality.—Incomplete repair of the ventricular septal defect results in a left-to-right shunt at ventricular level when the relief of the pulmonary stenosis has been sufficient to produce a pressure lower in the right than in the left ventricle.

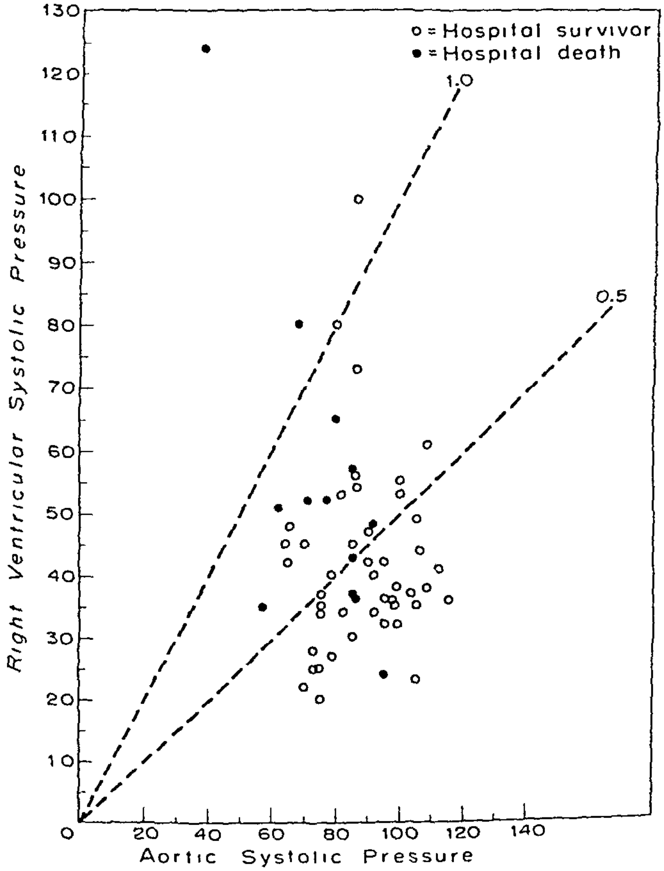

Fig. 1.—Degree of residual pulmonary stenosis as indicated by relation of the systolic pressure in right ventricle to the systolic pressure (mm. Hg) in aorta. Measurements were made in operating room after repair. All cases in which such data are available are included. High right ventricular systolic pressure resulted from incomplete relief of pulmonary stenosis, pulmonary artery pressure being low or normal in all cases.

It is reasonable to believe that this suddenly imposes a strain on the left ventricle and that systemic flow may be impoverished.

In 3 of the 21 patients who died in this series, there was an incomplete repair of the ventricular septal defect. In 2 of these 3, death occurred with progressing hypotension. It appears likely that the incomplete repair of the defect and consequent left-to-right shunt was a significant factor in these fatalities.

Associated Anomalies of the Coronary Arteries Related to Mortality.—Four patients had anomalies of the coronary arteries In Case 32, a large branch of the right coronary artery crossed the outflow tract of the right ventricle. At operation, the importance of this artery was not recognized and it was divided in making the incision into the right ventricle. The child died at the end of the operation and at necropsy complete absence of the left coronary artery was demonstrated.* Division of the branch of the right coronary artery supplying the left ventricle seems clearly the cause of death.

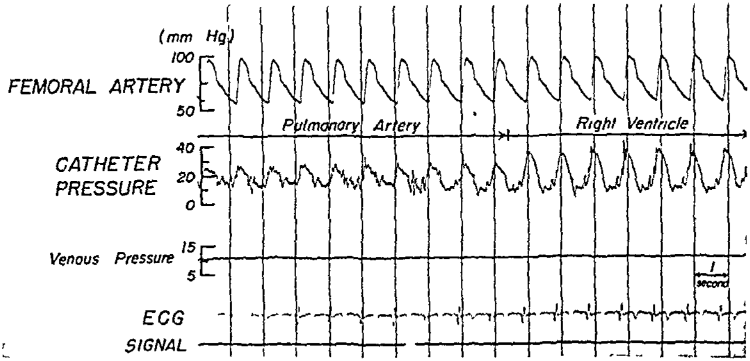

Fig 2 —(Case 57) Reproduction of photographic record of intracardiac pressures made in the operating room following closure of ventricular septal defect and relief of pulmonary stenosis by valvotomy and infundibular resection. Pulmonary artery and right ventricular pressures are recorded during withdrawal of the catheter from the pulmonary artery, the catheter having first been inserted through a needle into the lower part of the right ventricle and advanced into the pulmonary artery.

There remains only a 10 mm Hg gradient in pressure from pulmonary artery to low in *right ventricle This is considered a good result*

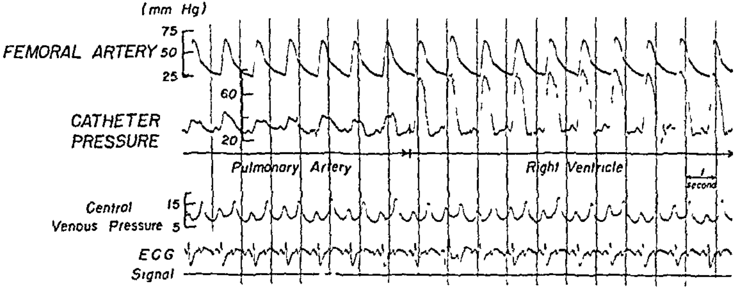

Fig 3 —(C [illegible] 'ographic record of pressures recorded as in Fig 2 Valvotomy a[illegible] quite inadequate in this case, since there was a large pressure [illegible] artery and right ventricle. Right ventricular systolic pressure [illegible] ic pressure Note elevated central venous pressure although [illegible] as judged by preoperative and postoperative weights. Patient [illegible]

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*For this and the other pathologic studies herein reported, we are indebted to Dr. J. E Edwards.

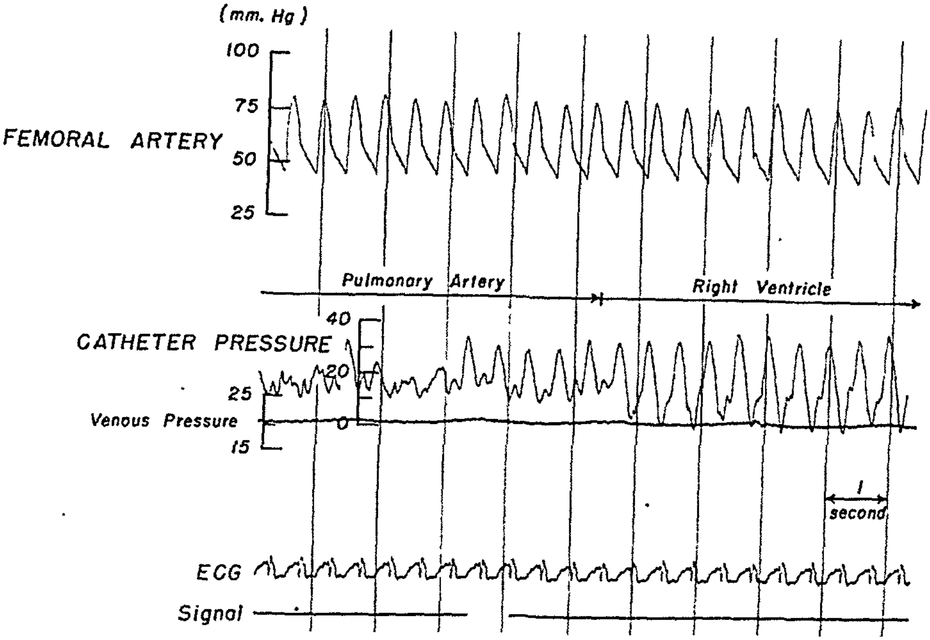

Fig. 4.—(Case 60.) Reproduction of photographic record of pressures recorded as in Fig. 2. Following valvotomy and infundibular resection, the very narrow right ventricular outflow tract and pulmonary valve ring were enlarged by reconstruction with polyvinyl (Ivalon) sponge. The good relief of pulmonary stenosis is demonstrated by the pressures recorded through the catheter during its withdrawal from pulmonary artery to right ventricle.

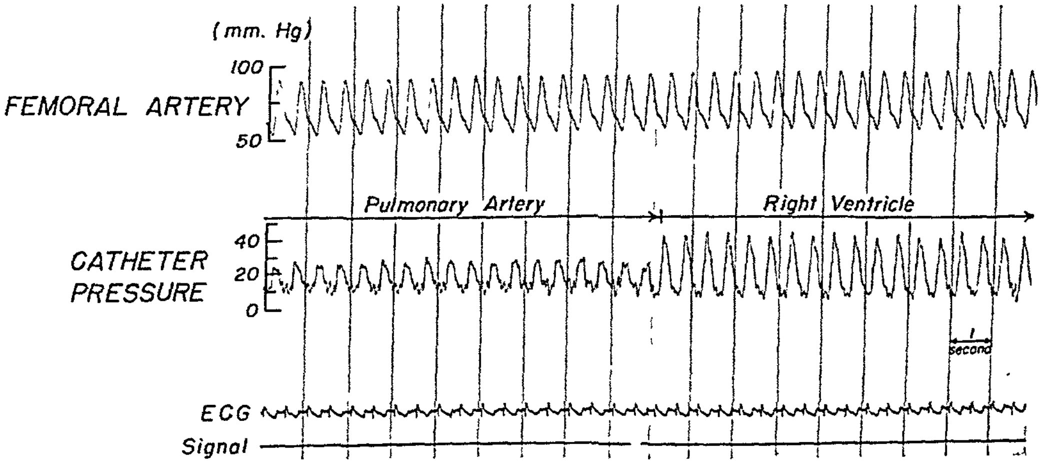

Fig. 5.—(Case 62.) Reproduction of photographic record of pressures recorded as in Fig. 2. Polyvinyl reconstruction was carried to bifurcation of pulmonary artery because of the very narrow outflow tract of right ventricle, narrow pulmonary valve ring, and diminutive pulmonary artery. The residual systolic gradient of 16 mm. Hg between pressures in the pulmonary artery and low right ventricle is considered functionally insignificant.

The lack of appreciable difference between the diastolic pressures in the pulmonary artery and right ventricle is related to the cutting through and Ivalon reconstruction of the pulmonary valve ring.

In Case 44, a large branch of the right coronary artery crossed the outflow tract of the right ventricle to supply the left anterior descending artery. Again, this was divided in the process of entering the right ventricle. The child died 48 hours after operation and the infarct demonstrated low in the left ventricle is considered to be the cause of death.

In the two subsequent patients with this finding at operation, the large anomalous branch from the right coronary artery was preserved. One (Case 52) made an uneventful recovery and the other (Case 56) died, presumably of other causes since the vessel was patent at necropsy and there was no evidence of myocardial necrosis.

Heart Block as Related to Hospital Mortality.—In 4 of the 21 deaths, complete atrioventricular dissociation in the postoperative period appeared to be a significant factor. One patient (Case 3), treated early in 1955 before supportive care for patients with heart block was well understood, died at the end of the operation. Another (Case 12) was placed on the artificial pacemaker a few hours after operation because of complete heart block which developed during repair of the ventricular septal defect. Adequate cardiac rate and systemic blood pressure were maintained for 10 hours, following which the heart no longer responded. Incomplete repair of the ventricular septal defect and incomplete relief of the pulmonary stenosis probably were also factors contributing to the death.

In Case 28, operation was done in haste because of poor perfusion, and relief of the pulmonary stenosis was inadequate. Complete atrioventricular dissociation was present when the heart resumed its beat after induced asystole, but this had changed to a 2:1 block by the time the incision was closed. Three hours after operation complete heart block was again present, but by then the child's general condition was very poor. She died 3½ hours later. Death had seemed inevitable even before the redevelopment of complete heart block.

The fourth patient (Case 64) died of what was probably heart failure 13 days after operation. It is believed that the complete atrioventricular dissociation which she had may have contributed to the cardiac failure although for the last 11 days of her life the ventricular rate was adequate without the use of an artificial pacemaker.

Left Ventricular Failure as Related to Hospital Mortality.—In the initial report on open intracardiac surgery from this clinic,[16] it was suggested that one patient (Case 1), with tetralogy of Fallot, died because the left ventricle was unable to accommodate itself to the suddenly enlarged pulmonary blood flow and pulmonary venous return.

Following this, left atrial pressure was monitored during operation [illegible] group of patients, and striking elevations were not noted after repair (T[illegible] IV). The highest left atrial pressure recorded by us in patients with [illegible]ished pulmonary blood flow prior to repair was in a patient who did [illegible] the tetralogy of Fallot. This boy had severe pulmonary stenosis [illegible] tricular pressure of 200 mm. Hg systolic, and right to left shunt across [illegible] ventricular septal defect. The left ventricle was diminutive. Left atrial pressure after repair was 24/12 with systemic venous pressure being 11 (mean). This patient survived.

Interpretation of the values for pulmonary and systemic venous pressure is difficult without rather exact knowledge of blood volume at the time the measurements are made. In early operations, blood volume was probably not maintained as constant as it has been in more recent operations. However, the values for left atrial pressure in the operating room following repair in these cases do not support a belief that left ventricular failure was present at that time. It is not at present believed that this is the explanation for the death in Case 1.

TABLE IV. LEFT ATRIAL AND SYSTEMIC CENTRAL VENOUS OR RIGHT ATRIAL PRESSURE (MM. Hg) IN OPERATING ROOM AFTER REPAIR OF TETRALOGY OF FALLOT

CASE	LEFT ATRIAL PRESSURE	CENTRAL VENOUS OR RIGHT ATRIAL PRESSURE
7	10/5	16/12
8	17/12	17/12
9	15/8	12/18
10	16/6	24/16
11	8/6	8
12	18/5	18/8
13	14/8	10/7
15	13/7	6/4
16	10/4	11/4
17	8/4	7/6
18	7/4	6
19	14/7	16/11
24	12/6	12/8
65	13/4	18/7
66	15/7	13/7
67	8/1	12/6

Since the first 5 deaths, only one patient (Case 56) has died with frank pulmonary edema. Left atrial pressure was not measured in the operating room in this case. The patient was not hypervolemic and weighed 320 grams less immediately after operation than before. Necropsy disclosed accurate repair of the ventricular septal defect. There was residual pulmonary stenosis. The perfusion had been in all ways standard and satisfactory. This patient had been profoundly handicapped prior to operation. He was not digitalized until after the onset of pulmonary edema which occurred about 4 hours after operation and persisted until death. There was also systemic hypotension which began about 2 hours after operation.

LATE RESULTS

Four of the 53 patients who survived operation and the postoperative period died after leaving the hospital. One (Case 33) died 6 months postoperatively of intractable Pseudomonas bacteremia and presumed bacterial endocarditis, having been operated on during the short period late in 1956 when this complication was occurring in some of our patients.[7]

A 5-year-old boy (Case 38) died at home 8 months after operation; he had been completely normal in all activities and appearance until he became suddenly ill with cough and respiratory distress and died 6 hours later. Sinus rhythm had been present at all times in the postoperative period and at dismissal. The *ventricular septal defect was repaired by direct suture and repair had seemed* complete and accurate. The ratio of right ventricular to aortic systolic pressure was 0.6 after repair. Unfortunately, necropsy was not obtained.

Another patient (Case 21) died 2 months after operation with a heart which was shown to be huge by roentgenogram of the thorax taken one week before death. As indicated in Table II, it is believed that grossly incomplete repair of the ventricular septal defect caused his death. In Case 34, death occurred at home of intractable right heart failure 2 months after operation which it is believed resulted from poor relief of pulmonary stenosis.

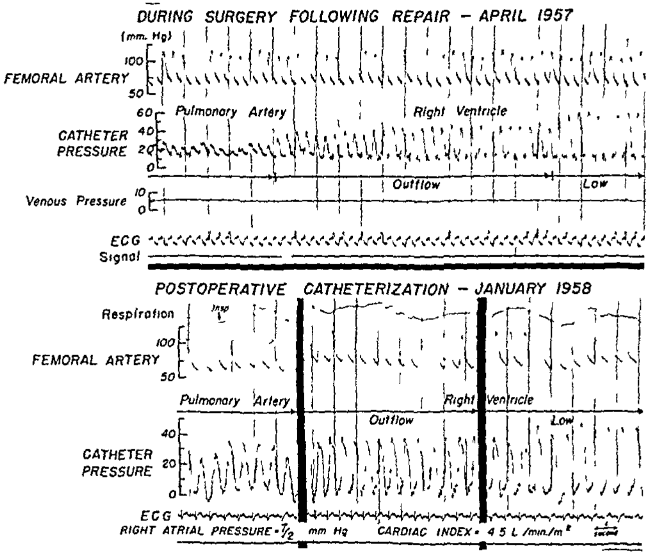

Fig 6.—(Case 41.) Comparison of [illegible] ery and right ventricle at operation and 9 months later at cardiac [illegible] ntricular systolic pressure is slightly lower 9 months later than it [illegible] repair. The ventricular septal defect was found to be completely [illegible]

Eleven patients (Case 63 through 74), although well when dismissed from hospital, were operated on too recently to allow evaluation. The remaining 38 patients are enjoying full activity and are completely without symptoms. None is cyanotic at rest or with exercise. This is in clear contrast to the pitiful preoperative status of most of these patients.

Of the 49 surviving patients, 5 are considered to have only fair relief of pulmonary stenosis but are asymptomatic. One operated on recently has had poor relief of pulmonary stenosis. Six have either evidence of or strong possibility of a small left-to-right shunt at ventricular level which to date has caused no symptoms in 5; the sixth (Case 69) was operated on too recently to allow symptomatic evaluation.

Postoperative cardiac catheterization has been done in only 7 cases. In only one (Case 39) was a residual small shunt demonstrated. In all, relief of pulmonary stenosis was quite satisfactory (Fig. 6).

PRESENT METHODS OF MANAGEMENT BASED ON THESE EXPERIENCES

Selection of Cases for Operation.—No patient with the tetralogy of Fallot is considered to be too ill for operation and a previous operative procedure is not considered a contraindication for operation. One surviving patient (Case 42) had had two previous operations; once a Potts anastomosis had been performed and, the second time, infundibular resection. Five other patients had undergone previous Blalock anastomoses. One other deeply cyanotic patient, not included in this report since she proved at operation to have atrial septal defect and pulmonary stenosis, previously had undergone a Blalock operation. Two of these 7 patients with previous anastomotic procedures died after operation, which included closure of the previously created shunt, one being the first one operated on in this series (Case 1) and the other (Case 14) dying from incomplete repair of the ventricular septal defect. The other 5 are well.

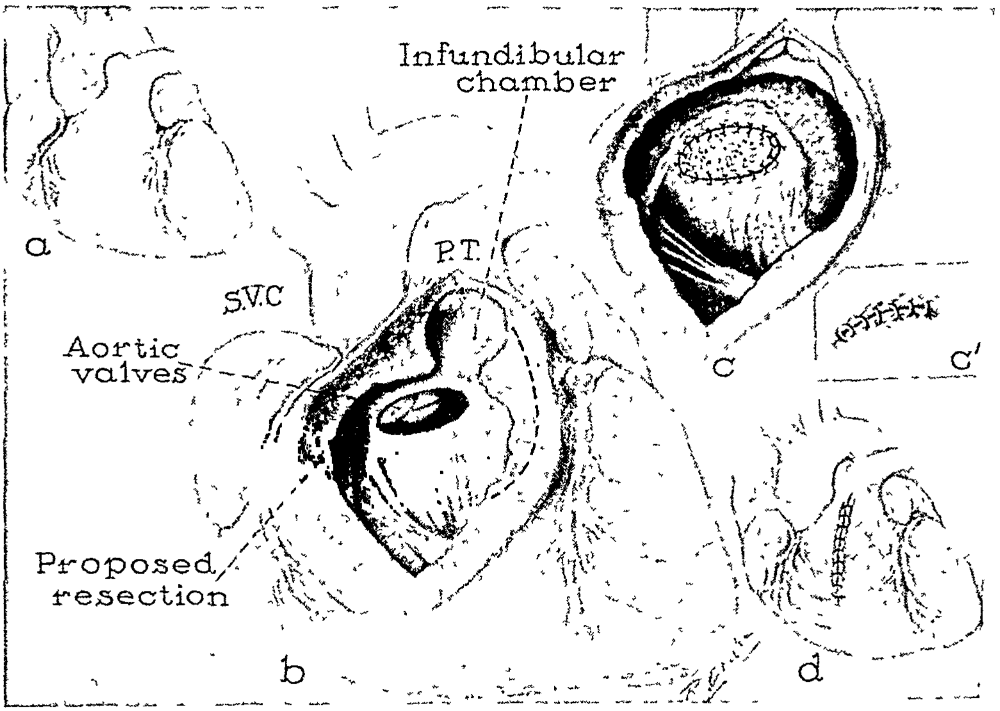

Fig. 7.—Open intracardiac repair of tetralogy of Fallot with infundibular chamber and wide pulmonary valve ring and artery. The unopened heart (*a*). The first step, after induction of cardiac asystole, is wide excision of the hypertrophied crista supraventricularis and relief of the infundibular pulmonary stenosis (*b*). Pulmonary valvotomy is performed when indicated. The ventricular septal defect is then repaired by direct suture (*c′*) or with compressed Ivalon sponge (*c*). If careful examination discloses a now adequate pathway through the outflow tract and pulmonary valve ring and artery, plastic reconstruction is not necessary *and the ventriculotomy is closed* (*d*).

Perfusion.—Accurate and complete intracardiac repair of the tetralogy of Fallot is time consuming in our hands. Thirty to 40 minutes of induced cardiac asystole and a total perfusion time of 40 to 70 minutes are usually required. In order that there be little or no mortality referable to the perfusion, it is believed that it must be conducted in an optimal way.[7] In the operations done in this series in the last 12 months, no deaths have been considered related to the perfusion.

The large bronchial flow and consequent large intracardiac return necessitates an adequate intracardiac sucker system as a part of the pump oxygenator employed. In all these cases, the system utilized[1] has allowed safe admittance of the aspirated blood to the general venous return and good visualization of the operative field.

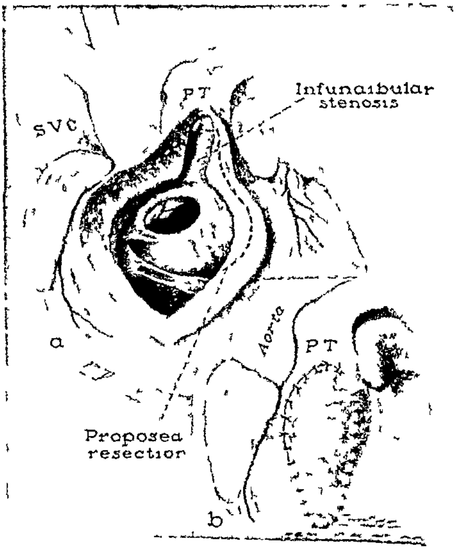

Fig. 8.—In cas
going to the valve ri
pathway. In such
struction and enlargement of the outflow tract (b)
row the incision and reconstruction is carried acr
chamb
a)
alo

Operative Technique.—The details
considered advisable for repair of the
9. Accurate visualization and repair
complished in a fashion similar to th
An Ivalon sponge prosthesis is oft
septal defect, although recently dir
In nearly all cases, infundibular
limbs of the crista supraventri
[illegible]

In light of the apparent relation between the adequacy of relief of the pulmonary stenosis and mortality, it is important to evaluate the cross sectional area of the outflow tract of the right ventricle, pulmonary valvular ring, and pulmonary artery. If it is clearly adequate for the accommodation of normal flow with minimal pressure gradient between the sinus portion of the right ventricle and the pulmonary artery, nothing further is necessary. If not, plastic enlargement is effected by the insertion of a curved, compressed, Ivalon sponge.

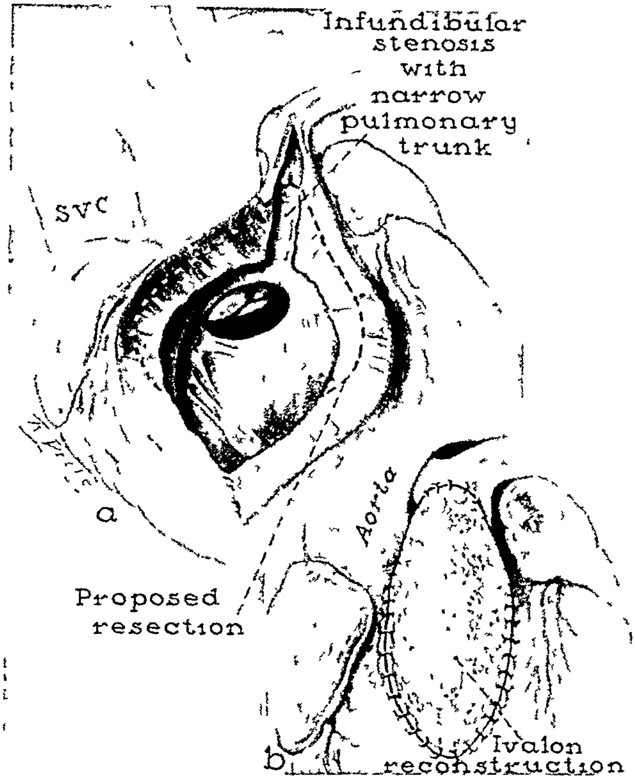

Fig 9.—A very narrow main pulmonary artery, or trunk, is sometimes present along with a narrow pulmonary valve ring and right ventricular outflow tract After infundibular resection, the incision must be carried to the bifurcation of the pulmonary artery and plastic reconstruction and enlargement of the *entire* area affected Note that the compressed Ivalon sponge is convexly curved to enlarge the cross sectional area beneath it.

Induced cardiac asystole is considered essential to accurate repair. It is probably important to abandon it after 40 minutes, leaving, if necessary, reconstruction of the outflow tract to be done with the heart beating. With the use of asystole, adequate exposure for the intracardiac manipulations can be obtained through a relatively small incision placed mostly in the outflow tract of the right ventricle. This may be advantageous with regard to cardiac function in the postoperative period.

Associated lesions, such as atrial septal defect or patent ductus arteriosus, must be identified and repaired. Where there is a large anomalous branch of the right coronary artery, decision as to procedure is difficult. It appears unwise to sever it. In such a case, if good relief of pulmonary stenosis is possible without a plastic reconstruction of the outflow tract, the operation should proceed as planned, extending the incision only up to this vessel. If adequate relief of the pulmonary stenosis is impossible to achieve in this fashion, the plans for proposed complete intracardiac repair probably should be abandoned and either isolated infundibular resection or an anastomotic procedure performed.

Postoperative Care.—Administration of fluid is managed as in other cases after intracardiac surgery.[18] Patients are kept in an oxygen tent with a humidified atmosphere for 48 to 72 hours after operation. The most important decision to be made concerns administration of digitalis. It is believed not advisable routinely to bring these patients to surgery digitalized, nor routinely to administer digitalis in the postoperative period. When the pressure [illegible] right ventricle remains moderately elevated after repair, digitalization [illegible] day of operation has proved beneficial. Also, should hypotension or [illegible] pulmonary edema develop, digitalis should probably be administer [illegible]

Many patients are not digitalized in the early postoperative [illegible] some of these, retention of fluid and hepatomegaly insidiously [illegible] come apparent 10 to 14 days after operation. Restriction of [illegible] tion are instituted and maintained for 4 to 6 weeks, followin- [illegible] difficulty has developed.

When complete atrioventricular dissociation and [illegible] occurred, isoproterenol hydrochloride (Isuprel) and the [illegible] employed as they are after repair of isolated ventricul [illegible] managed, heart block should rarely be a cause of [illegible]

SUMMARY

Experiences with open intracardiac rep [illegible] described together with details concerning [illegible] and late mortality. The operation, [illegible] must be done with precision if the bes [illegible]

The excellence of the late results [illegible] operative mortality render open in [illegible] the tetralogy of Fallot. A longer [illegible] quired finally to establish whe [illegible] lesion. Yet it is, in the opinio [illegible]

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DISCUSSION

DR. RICHARD A. RASMUSSEN, Grand Rapids, Mich.—We all admire the results obtained in the successful case of tetralogy of Fallot when corrected by the direct anatomic method. This is the condition which Dr. Blalock first treated successfully in 1945. Dr. Kirklin and his co-workers at the Mayo Clinic are to be commended for this presentation. It is recognized that true anatomic correction is our aim but this cannot always be attained in the problem of decreased blood flow. It must be remembered that there are other far less hazardous procedures which do give a good physiologic result, and these may still be considered for certain selected types of cyanotic heart disease, especially when the risk is great.

In the April issue of the JOURNAL OF THORACIC SURGERY, Dr. Sanger and his associates of North Carolina suggested the use of a vena caval-pulmonary artery anastomosis to increase the pulmonary blood flow. This procedure would also decrease the work load of the right heart. They presented experimental data indicating the feasibility of the procedure. I and my associates would like to report the use of a superior vena caval-pulmonary artery anastomosis for transposition of the great vessels with pulmonary stenosis. This was done in a 17-month-old boy who at 4 months of age began to have severe cyanosis with episodes of unconsciousness. These spells became more severe and frequent over a period of one year, until he was admitted to Blodgett Memorial Hospital for diagnosis and treatment, having been in oxygen for one month. Consideration was given to the various shunting procedures that might be done on this child On exploration on April 24, 1958, the anatomic findings and additional pressure studies confirmed the diagnosis of transposition and pulmonary stenosis It seemed that a superior vena caval pulmonary artery shunt would be ideal for this patient, and this was done

(slide) This is an x ray photograph which demonstrates the shape of the heart, the decreased pulmonary vasculature, and the aorta which arises from the right ventricle, and the pulmonary artery probably arising from the left ventricle

(slide) This is a sketch showing the findings at operation as described Note the transposition and the pulmonary stenosis We simply disconnected the superior vena cava from the right auricle and connected it directly to the disconnected distal end of the right pulmonary artery after the latter had been severed at its origin from the main pulmonary

(slide) This is the result one week later Note the good color

The immediate result of this procedure seems to be excellent The increased oxygen saturation changed from preoperative catheterization values of 59 per cent to 83 per cent immediately following surgery The color improved immediately It should be pointed out that the superior vena cava blood bypasses the right heart completely and therefore eases the work of the heart The increased blood flow through the right lung undoubtedly accounts for the increased oxygen saturation and the clinical improvement The procedure was well tolerated in a poor risk case The operation is essentially a continuous perfusion of the right lung It has a real advantage over the other shunting procedures in that the strain on the heart is decreased instead of increased

From the success in this case it would appear that the physiologic studies of Sanger and associates are confirmed in the human being It is hoped that others will consider and try this new shunting technique for poor risk cases similar to the one reported, and other similar problems of decreased pulmonary blood flow

DR FRANK L GERBODE, San Francisco, Calif —I want to speak of one point Dr Kirklin made about the left to right shunt which results after reopening of a septal defect following repair of a tetralogy of Fallot We have operated upon 14 patients now with tetralogy of Fallot and we have 10 living Three patients died because of difficul with outflow tract problems, and I must confess we were not as good as Dr Kirklin [illegible] in taking care of them I wish particularly to speak of one patient, an adult, wh [illegible] a tetralogy of Fallot He had a perfectly adequate operation, we thought, with re [illegible] ig out of the outflow tract and repair of an interventricular defect with an Ivalon pro [illegible] is On about the tenth postoperative day, it was quite obvious that the interventricula [illegible] defect had opened That resulted in a truly colossal left to right shunt The calcula [illegible] shunt flow was something like 30 L in this boy He developed an enormous hea [illegible] gallop rhythm, and all the evidence of acute heart failure It seemed as though fa [illegible] re blood passed through the shunt than one might expect from a defect of this size [illegible] flow suggested that some mechanism was not present in the lungs, which might hav [illegible] een present in an ordinary interventricular defect, a mechanism which perhaps protects against a flow of this magnitude under such circumstances In any event, after a month we took the boy back to the operating room and found that the Ivalon prosthesis had separated on one side We were fortunately able to close it successfully and I am glad to report that he is well But I must say that the second operation, after a month, was fraught with certain difficulties, because enough time had elapsed to vascularize the adhesions, and hemothorax and hemocardium required another operation After the experience in this case, and in one other, I would suggest that if failure is evident, perhaps an earlier intervention at 2 or 3 weeks might be indicated

SIR RUSSELL C BROCK, London England —In the very short time available for discussion it is impossible to do more than make straight comments and observations without supporting argument

Even after the magnificent papers we have listened to I do not think the problem of the so-called corrective treatment of Fallot's tetralogy has been settled. We are told that the complex problems of the smallness of the pulmonary outflow tract can be solved by sewing a large piece of plastic material either into the wall of the infundibulum or, even more disturbing, across the pulmonary valve ring and into the wall of the pulmonary trunk. This procedure has several grave disadvantages and I feel we are in danger of being misled by the brilliance of the pure technical achievements now permitted by successful "heart-lung bypass," we are in danger of ignoring certain fundamental surgical principles which, I feel, cannot be ignored.

The introduction of foreign substances into the body is rarely acceptable, safe, or satisfactory as a long-term policy. A piece of inert material buried in some relatively inactive part of the body *may* give no trouble. But here it is proposed that it is safe, and is sound surgery, to introduce foreign material into one of the most active parts of the body—the outflow tract of the right ventricle. Moreover, in one third of the cases this substance is astride the pulmonary valve which is thereby rendered totally regurgitant. I find it difficult to believe that a foreign substance, constantly exposed to such severe mechanical strains, will not give rise eventually to serious trouble. This is quite apart from the inevitably harmful effects of total pulmonary regurgitation.

This technique also ignores the fact that the disproportion between the two circulations is more extensive than the pulmonary outflow; it extends to the balance of power and distribution of effort of the two ventricles.

I find it difficult to believe that this technique is an acceptable solution to the problem of the correction of the smallness of the pulmonary outflow tract.

I suggest that there is an alternative method of increasing the size of the outflow tract more physiologically, that is by giving nature a chance, by encouraging the natural process of growth. This process is inevitably related to function and can be achieved by a preliminary direct operation to relieve the pulmonary stenosis, whether it be valvular or infundibular or both. When sufficient time has elapsed to enable the pulmonary outflow to develop and the balance of the ventricles to be more happily adjusted, then the septal defect can be closed by a second stage.

I am second to none in agreeing that, whenever possible, a single-stage, totally corrective operation should be done for Fallot's tetralogy. Fallot's tetralogy, so-called, is, however, *not a disease entity*, is *not* a homogenous group. The label covers a whole range of conditions of abnormal development, and to apply one standard method of operation to all seems to lack finesse. I believe that for these very difficult types of Fallot's tetralogy in which the pulmonary outflow is so small and the disproportion between the aorta, the pulmonary vessels, and the two ventricles is so extensive that some form of two-stage operation is necessary, the first, or preliminary stage should relieve the stenosis; the second stage will consist of closing the septal defect.

Time alone can tell whether a standard one-stage corrective procedure is possible. Because these patients leave the hospital apparently well does not convince me that they will continue well for the remainder of the long life that should lie before them if they have in truth been "totally corrected and cured." I leave to you the simple thought that in some of these cases there is and will always be a place for some form of two-stage, gradually corrective procedure.

DR. WILLIAM W. L. GLENN, New Haven, Conn.—I would certainly like to express my very great admiration of Dr. Kirklin's and Dr. Lillehei's magnificent work in the correction of the tetralogy of Fallot. The direct correction of this lesion is obviously the procedure of choice when possible. We have been interested in the problem of the occasional case of the tetralogy that cannot be corrected by the direct procedure and, particularly, in other patients with conditions characterized by malfunction of the right side of the heart where correction by direct technique is either not possible or is unsatisfactory.

About 3½ years ago, in 1954, we reported our first experience with the application in the experimental animal of a procedure similar to that just described by Dr Rasmussen A shunt was made between the superior vena cava and the distal right pulmonary artery After extensive experimental trial, this operation was applied to a patient with a single ventricle pulmonary stenosis in transposition of the great vessel (slide) This slide shows an angiogram of a child 7 years of age who had this combination of defects and where the distal end of the right pulmonary artery was anastomosed to the side of the superior vena cava and the superior vena cava was then ligated just above the right auricle This angiogram was made 2 months following operation, which was done in February, 1958 It shows the dye injected into the left brachial vein entering the superior vena cava, then the distal right pulmonary artery bypassing the right side of the heart The dye then passed rapidly through the lung, the pulmonary veins, and into the left auricle

I would like to point out particularly that this procedure is fraught with great hazard if thrombosis of the anastomosis should occur It should therefore be done only in preference to other corrective or palliative procedures where the indications are exceptionally clear I should like to emphasize, also, that the procedure should not be performed unless the pulmonary artery pressure is low or certainly normal, but never where it is elevated, and it should be performed only when the vessels concerned, the pulmonary artery, and the superior vena cava, are of large size

DR C WALTON LILLEHEI, Minneapolis, Minn —Tetralogy of Fallot is a curable malformation! Our experiences of the past 4 years demonstrate that unequivocally Moreover, the complete correction can be carried out in consecutive patients unselected other than by virtue of the fact that they are "in trouble," with an immediate operative risk comparable to and even less than that possible with the palliative procedures And, beyond this it is in the months and years following operation that the great dividends of restoring the circulation to normal are returned with compounded interest

In the beginning in 1954, due to the learning phases inherent in the development of both new perfusion methods as well as new operative techniques for a complex defect, the immediate operative risk was higher for the complete correction than for the palliative procedure However, even then this increased risk was more apparent than real for, in the first 10 patients to have the curative procedure, there were six successes and four deaths (Ann Surg 142 418 445, 1955) In the 3½ years that have elapsed since this first series was treated there has been no late mortality among the successful cases and, in fact, none of these 6 patients has had any cardiac difficulty whatsoever Most have now been restudied objectively and proved to have normal physiology Thus, even this initial mortality of 40 per cent compares quite favorably with the 30 per cent death rate noted in a series of 110 shunted patients followed 2 to 10 years (Arch Surg 75 928 945, 1957) Moreover, in this latter series an additional 16 per cent were alive but unimproved and obvious candidates for another operation

Therefore, at the present time, when the curative procedure can be carried out with an operative risk of 10 per cent or less and the late mortality can be expected to be negligible, there is not the slightest doubt as to the procedure of choice

As a result of this and numerous other therapeutic gains, the field of intracardiac surgery is a burgeoning specialty The transition from extracardiac to intracardiac techniques requires not only broad operative experience in thoracic surgery but a dedicated interest and knowledge as well of the known and experimental aspects of the physiology of respiration and circulation, not to mention cardiology Thus, no wonder one finds now and then traces of doubt expressed by some surgeons beset with early failure However, this lack of courage upon their part to carry through can be expected to pass

At the 1958 Meeting of the University Surgeons in February, we sought to analyze our experiences in the surgical treatment of the first 100 patients with the cyanotic variety of tetralogy and five factors stood out as important contributions to the significant reduction in risk which has occurred. I should like to show this slide which summarizes these as follows:

1. *Efficient Perfusion.*—Our average cyanotic tetralogy patient requires a 60-minute perfusion for a curative operation. Arterial blood pressure is continuously monitored and is maintained at a normal level by adjusting the flow rate accordingly. Here, in respect to pressure maintenance, is one of the values of using an occlusive pump. Hemolysis, as Dr. Hodges has pointed out in the Forum, has virtually nothing to do with whether a pump is occlusive or nonocclusive, but maintenance of flow against resistance does.

The metabolic efficiency of the helix reservoir bubble oxygenator has been an important factor contributing to routine success in these longer perfusions. Especially important are its safety factors related to sterilization of all parts in contact with blood by autoclaving, and the fact that the entire extracorporeal circuit except for a few easily cleaned stainless steel connectors and adaptors is disposable. It is surprising to me that in 1958 some surgeons are still working with equipment that cannot be heat sterilized and is not only *not disposable* but of design difficult to clean. In addition, some of the film oxygenators in use require significant quantities of saline, albumin, dextran, or P.V.P. in order to function. It is no wonder then that, under such circumstances, patients are lost due to such complications as infection, hemorrhage, and pulmonary or cerebral edema.

Moreover, gadgeteers obviously with more money than physiologic background are still equipping pump oxygenators with various electronic level sensing devices that, in situations of duress, function solely to maintain the machine's blood volume at the expense of the patient's. Nothing could be more ill conceived.

2. *Ventricular Defect Closure.*—In tetrad patients, a prosthesis is necessary very frequently. The defects are usually large and their margins of soft, red muscle will not hold stitches for long under any tension.

3. *Right Ventricular Outflow Tract Reconstruction.*—The severity of the stenosis is widely variable as must be the surgical techniques to relieve it. However, in the severe cases the sine qua non of success is the use of an outflow roof as previously described (Arch. Surg. 73:526-531, 1956). In a few very severe hypoplasias of the bulbis cordis region, it is necessary to continue the outflow roof across the annulus into the main pulmonary artery.

4. *Selective Cardiac Arrest.*—Elective asystole with potassium citrate has proved very valuable in the tetrad group, but must be used *selectively* for best results. That is, induced only if necessary in that particular case and, then, only for as long as absolutely necessary. The duration of arrest is best kept under 30 minutes. We used to vent the left atrium with a catheter in all tetralogy patients (Extracorporeal Circulation, Springfield, 1958, Charles C Thomas, publisher, pp. 41-56) but this is now accomplished by the simpler method of releasing the aortic clamp early enough to allow the ventricular defect itself to act as a vent while the ventricular patch is being seated and the stitches tied.

5. *Complete Heart Block.*—In the present state of our knowledge it has been impossible to avoid this complication in 10 to 15 per cent of tetralogy patients. Surgeons who say they have no heart block problem are simply not doing much surgery of this type. Fortunately, the myocardial electrode with internal pacemaker stimulation handles the situation very well until sinus rhythm returns or adaptation to the slower rate has occurred. The next advance is to learn how to avoid block completely.

DR. KIRKLIN (Closing).—I should like to thank Dr. Rasmussen and Dr. Glenn for giving us their experience and their views on this subject. Perhaps I might be permitted to comment specifically on Dr. Gerbode's discussion and that of Sir Russell Brock. It is pertinent I think to emphasize again what Dr. Gerbode has said, namely, that if one relieves the obstruction to outflow from the right ventricle by a reasonably good operation, and leaves the ventricular septal defect open, the residual shunt does not continue to be right-to-left, but becomes, suddenly and overwhelmingly, left-to-right. I think this is obvious. Along the same line one must remember that if one makes a complete repair of the ventricular septal defect there is suddenly a markedly increased pulmonary flow In other words, the right ventricle is now ejecting all its blood across the pulmonary valve, whereas prior to that, of course, it was ejecting a good deal of it across the ventricular septal defect The right ventricular pressure is a function not only of that resistance but also of the flow, and when flow goes up an opening which has been only moderately increased in size by the operation it may produce a right ventricular pressure which is the same as it was before surgery, or indeed higher So one must open this area widely

I was privileged to discuss a month or so ago with Sir Russell Brock this problem of the outflow tract, and I think his comments and his admonitions must be very carefully considered Personally, I agree completely that any foreign substance anywhere in surgery is undesirable and should be avoided if possible I suppose I am particularly concerned about something like compressed Ivalon sponge, which is fairly leathery and which probably is not incorporated within tissues

I agree that it might not be a very important technical point whether one repairs the ventricular septal defect by direct suture or sponge, but if both are equally satisfactory then it must be better without a sponge since we have no foreign material In the outflow tract however, it appears necessary in some cases to make some sort of plastic reconstruction I suppose then we must accede to the possible objection that this is the Achilles' heel of this particular operation Still, we have no evidence as yet, as Dr Lillehei pointed out, after 2 years of experience, that any one of these patients has had late trouble One thing that perhaps worries me a bit about a two stage procedure as suggested by Sir Russell, is whether the very small fibrous pulmonary valve ring, not the outflow tract, not the main pulmonary artery, but this very small ring, would enlarge significantly with the resection of the fibrous tissue beneath it Perhaps it will, I do not know I think we have to admit that this is not yet a completely settled point, but I do think we have a right to assert that in the 2 years at least that these patients have been followed there have been no ill effects

ATRIAL SEPTAL DEFECT, SECUNDUM

An Analysis of One Hundred Patients Undergoing Open Surgical Repair

Henry Swan, M.D., Allan B. Kortz, M.D. (by invitation), D. Hywel Davies, B.M., M.R.C.P. (by invitation), and S. Gilbert Blount, Jr., M.D. (by invitation), Denver, Colo.

OUR TOTAL experience with the open repair of interatrial septal defects of the so-called secundum variety is now somewhat in excess of 100 cases. In addition, we have treated 20 patients with pulmonary valvular stenosis, associated with patent foramen ovale or atrial septal defect, and a few others with septum primum or atrioventricularis communis. Because of the important differences in the pathologic anatomy and physiology which occur in the presence of these latter anomalies, it seemed wise to confine the subject of this report to a study of those patients who had some variant of the secundum-type lesion, and who did not have pulmonary outflow obstruction. This paper, therefore, concerns the first 100 consecutive patients recommended for surgery and proved to fit into this category at open-heart operation.

SURGICAL BACKGROUND

The history of the operative repair of atrial septal defect has been typical of the recent rapid development of cardiac surgery in general. Groupings for usable techniques and tolerable cardiac manipulations were made in the experimental laboratories after the methods for thoracic exploration in general became understood. Attempts to create an experimental preparation which simulated the clinical defect were soon successful and, using this preparation, actual methods for closed, or nonvisual, repair were soon elaborated. Some of these were crude while others became more refined and, in fact, are still in use today in a few centers. Meanwhile, the effort to develop techniques for the visualization of operative fields inside the heart was vigorously pursued in many laboratories. The first method for open-heart surgery to achieve a degree of safety which warranted application to the human was hypothermia,

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From the Departments of Surgery and Medicine, University of Colorado School of Medicine, Denver, Colo.

Aided by grants from the United States Public Health Service and The American Heart Association.

Read at the Thirty-eighth Annual Meeting of The American Association for Thoracic Surgery at Boston, Mass., May 16-18, 1958.

and for 3 years before the use of cardiopulmonary bypass became generally available, we gained experience with this technique and solved many of the problems encountered in the open operative repair of atrial septal defect. At present, then, widespread trial of both hypothermia and cardiac bypass is being made in various centers throughout the world. Since by the time the heart-lung machine became available, hypothermia had been developed in our clinic to a degree of safety approaching a risk of zero, and since the operation had proved so effective, we saw no reason to discontinue this method. In the long run, the choice of technique will emerge in terms, first, of safety to the patient and effectiveness of the operative procedure; then, of simplicity, cost, and blood banking problems. In the present series, all of the operations were performed during circulatory arrest while the patient was in a state of hypothermia.

The first studies contributing to the story outlined above are those which evolved a technique for the temporary interruption of blood flow through the heart. It is surprising that this method, first described experimentally by Haecker[1] in 1907, was apparently not used clinically until Swan, in 1949, applied it to the open removal of foreign bodies in the heart[2] and the closed repair of atrial septal defects.[3] Haecker's work was soon confirmed by both Sauerbruch[4] and Rehn. It was soon established by Liewen and Sievers[6] that, in rabbits, inflow occlusion was much better tolerated than outflow occlusion. Survival roles following various durations of inflow occlusion in animals at normal temperatures have gradually become established, and the concept of a rapidly rising mortality after a short safe period has emerged. As a result of experiments by Scheppelman, Carrel,[8] Tuffier,[9] O'Shaughnessy,[10] Adams and Escudero,[11] Shaw and co-workers,[12] Templeton and Gibbon,[13] Cohen,[14] and Swan[15] and their associates, it became apparent that all dogs will survive 1½ minutes of occlusion, most dogs will tolerate 5, whereas the majority will succumb if the period is lengthened to 10 minutes.

Various measures to increase the safety of long- or middle-range occlusion have been suggested. Brain perfusion[6, 10] was not successful. Hyperventilation[14] before occlusion and hexamethylamine[16] were suggested but not widely adopted. Adams and Escudero,[11] in their important study, felt that a gradual return of work load to the heart following occlusion in the middle range helped reduce the incidence of cardiac death. They demonstrated that more blood returned to the heart via the inferior vena cava than via the superior vena cava; occlusion of the former alone caused a 60 per cent drop in carotid artery pressure, while occlusion of the latter caused only a 30 per cent drop. They recommended, therefore, release of the superior vena cava first, followed after a few minutes by release of the inferior vena cava. Thus, the overdistribution caused by a sudden large flow of blood presented to the hypoxic heart is prevented.

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The influence of hypothermia on the tolerable limits of inflow occlusion has been extensively studied and the reports are too numerous for review in this paper. In spite of these studies, however, there is still no general agreement concerning the survival limits in man for the brain and for the heart during cardiac inflow occlusion at various levels of decreased body temperature. Nonetheless, it is apparent, both experimentally and clinically, that hypothermia has lengthened the "absolutely safe" period of inflow occlusion by a sufficient amount to be eminently practical for intracardiac procedures not exceeding 10 minutes in duration.

The development of a method for the experimental creation of interatrial septal defects was an important preliminary to the evolution of techniques for repair. Simple incisions and small excisions of atrial septum promptly heal (Martin and Essex,[17] and Dodrill[18]). Blalock and Hanlon[19] created a persistent defect, but one which lay anatomically above and posterior to the usual clinical lesion. Using the inflow occlusion principle, Swan[15] created large defects in the mid-septum by direct-vision excision. These defects allowed the elaboration and evaluation of techniques for closure. Other methods for creation of the defects were subsequently devised (Hufnagel and Gillespie,[20] Donald,[21] and Gross[22] and their co-workers) and from these studies techniques for closure were suggested.

The first experimental attempt at repair of an atrial septal defect, however, was that of Cohn in 1947,[23] using a patch of auricular wall. Swan,[15] in 1950, suggested the inversion of the auricular appendages through the defect, thus attempting to plug the hole. Although this was only partially successful, a principle was established which later proved of importance. This was the concept of the "doughnut-lumen" of the auricles, which it was shown did not interfere with the flow of blood from the venae cavae to the tricuspid valve. This principle was applied clinically in 1950, and on May 6, a 9-year-old patient was operated upon, using this technique, at the Colorado General Hospital. It is believed that this patient is the first individual to survive an attempt at surgical repair of an interatrial septal defect. (He has subsequently had successful open closure of the residual defect.) The principle of the "doughnut-lumen" was later utilized by Bailey and his colleagues in 1952,[24] who modified the technique to involve suture of the lateral wall of the auricle rather than the appendage, and by Shumacker and his associates,[25] who added to the procedure a sac made of pericardium or plastic materials attached to the auricular wall.

Meanwhile, another variation of the patch idea of Cohn was being explored. Instead of a part of heart muscle, inert plastic buttons were examined to see if they would not excite undue thrombosis and to determine their fate when sutured to the wall of the auricle. Hufnagel and Gillespie, in 1951,[20] described an ingenious method for the application of two nylon buttons. Swan and Stewart, in 1953,[26] described a modification of the original "button" technique which left a polyethylene sheet over the defect inside of the right auricle and, in this publication, described the remarkable process which first covered the plastic with fibrin and then, by the process of endothelization, converted the fibrin envelope to a smooth glistening membrane completely surrounding the polyethylene prosthesis. Later, Donald and associates,[27] using polyvinyl sponge, Miller and co-workers,[28] Pomeranz, Watkins and Gross,[29] and Bahnson and Baker[30] studied a variety of tissues and plastic materials implanted in the heart. These experiments demonstrated the important fact that, whereas pericardial grafts or other autogenous or homologous free tissue grafts excite thrombosis and are replaced by fibrous scars, a variety of plastic materials are well tolerated in the lumen of the auricle, and excite processes which result in their becoming completely encased in a smooth, endothelized membrane. Utilizing this principle, Kuklin and co-workers[31] reported a successful clinical series, in 1955, placing the polyvinyl sponge across the defect by means of the Gross "well."

Another technique for the closure of septal defects, namely, a circular suture passed outside of the heart around the defect was suggested by Murray in 1948,[32] and subsequently developed by Sondergaard[33] experimentally, and given clinical trial by Bjork and Crafoord.[34] A large suture, in this technique, is passed through the upper edge of the ventricular septum or the lower portion of the atrial septum and then tied down in a previously developed plane between the right pulmonary veins and the posterior aspect of the right atrium, thus squeezing closed the entire atrial septum. It is obvious that this technique, while possible for the simpler defects, is not anatomically suitable for the more complex lesions with aberrant pulmonary veins.

Meanwhile, a direct vision attack, in 1953, was achieved first by Lewis and Taufic[35] after considerable experimental work in the laboratory utilizing hypothermia, a principle of inflow occlusion and open atriotomy with direct suture of the defect. Shortly thereafter, we also undertook a study of this method[3] clinically, and this report comprises our observations on the use of this method in our first 100 patients treated in this fashion.

ANATOMY

The embryology of the atrial septum has been so well described by Rokitansky[36] and by Patten[37] that the terminology has been universally adopted. In the latter's opinion, the septum secundum defects result from either normal development of the septum secundum with excessive resorption of the valvula foraminis ovalis, or arrest in the development of the septum secundum with failure to reach the caudal margin of the ostium secundum. A further degree of classification would have some clinical merit if it helped the surgeon understand the variations of the anatomy encountered. Kuklin,[31] Lewis,[38] and Bedford[39] and their co-workers have discussed this problem. Our own classification is in general agreement with all three authors, but differs from other systems in our distinction between so-called "primum" defects and atrioventricularis communis. This classification follows:

I. Interatrial septal defect, secundum
   A. Foramen ovale defects
      1. Foramen ovale open due to defect in valvula foraminis ovalis which may be partially present as a caudal or dorsal margin, or as a fenestrated membrane.

2. Valvula foraminis ovalis absent; lower margins apparently continuous with valve of inferior vena cava. Anomalous pulmonary venous drainage may be associated with this defect.

B. Septum secundum defects (high).
These defects are situated immediately inferior to the entrance of the superior vena cava; they usually have no cephalic or dorsal margins; they are often associated with anomalous return of pulmonary veins from the right lung to the right atrium or superior vena cava, or with anomalous pulmonary venous return from the left lung into a left superior vena cava and/or a coronary sinus.

C. Combined defects.

II. Interatrial septal defect, primum.
These defects, which are very rare, are situated in the lower portion of the septum; there is no inferior margin above the upper edge of the ventricular septum, *but also there is no defect or cleft in either of the atrioventricular valves.*

III. Atrioventricularis communis.
1. The atrioventricular cushion is intact and the "ventricularis" part of the defect consists only of a cleft in a mitral or tricuspid leaflet.
2. A frank defect in both septa is present.

Evolution of this classification was stimulated because of the clinical importance of distinguishing lesions not amenable to short open-exposure correction. The characteristic aspect of atrioventricularis communis is the presence of incompetence of one or both atrioventricular valves. This phenomenon results in a very different alteration in hemodynamics and thus a very different clinical entity than with atrial defect alone, where the valves are both competent. Thus, the hypertrophy of the left ventricle, the lack of marked right-sided preponderance in the electrocardiogram, and the presence of a blowing systolic murmur heard best at the apex or just to the left of the sternum in the fourth and fifth interspaces are distinctly at variance with the findings in defects of the atrial septum alone. Moreover, since the septal leaflets of both the mitral and tricuspid valves embryologically are derived from the tissue which also forms the ventricular septum, a congenital defect of these structures, it seems to us, should be considered as a variant of ventricular rather than atrial septal development. When associated with a hole in the atrial septum, such a combination is truly atrioventricularis communis, in its mildest form.

TABLE I. DISTRIBUTION OF ANATOMIC TYPES OF ATRIAL SEPTAL DEFECTS AND THEIR ASSOCIATION WITH ANOMALOUS PULMONARY VENOUS DRAINAGE

TYPE OF LESION	NUMBER	NUMBER WITH ANOMALOUS PULMONARY VEINS
Foramen Ovale Defects		
1. Defect in valve	77	2
2. Valve absent	9	4
Septum Secundum Defects	12	10
Combined Defects	2	0
Totals	100	16

With this classification, then, septum primum defects become extremely rare. Most lesions which others might classify in this fashion are associated with a mitral cleft and thus we classify them as a variant of atrioventricularis communis. On the basis of this classification, the distribution of cases in this series is presented in Table I.

CLINICAL MATERIAL

The first patient in this series was a 26-year-old woman who was operated on April 15, 1953; the one hundredth was an 8-year-old girl operated on Jan. 14, 1958. The age span was from 10 months to 45 years, distributed as shown in Fig. 1. The jump in incidence in the 6- to 10-year group may be a function of school entrance examinations at age 5 or 6. The large number of relatively old patients coming to surgery for a congenital defect reflects the lack of a previously available method of repair. A large backlog of untreated patients exists in the population. It is to be hoped and expected that as the years go by, with greater awareness of the desirability of early treatment on the part of physicians in general, most of the patients with this disease will be recognized at grade school age and referred for treatment when the operative risk is very low, in fact, roughly equivalent to that for repair of patent ductus arteriosus.

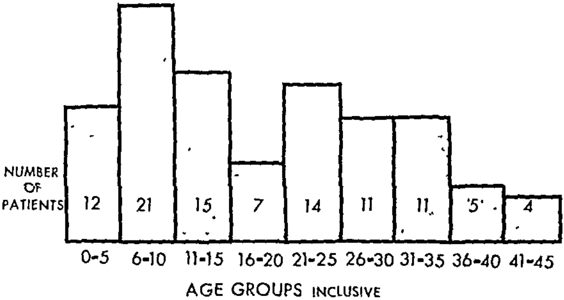


Fig. 1—Age distribution at surgery for atrial septal defect (100 cases).

It is worth noting that the influence of sex on the incidence of this disease is quite pronounced. Our experience is similar to that reported by many others. We had 68 female patients, as compared to 32 males. Since roughly two out of three defects occurred in females, the sex of the patient becomes a minor factor in the diagnosis.

THE NATURAL HISTORY OF ATRIAL SEPTAL DEFECT

During fetal life, the presence of an atrial septal defect places no increased burden upon the circulation, as the normal blood flow passes from right atrium to left. Following birth, a left-to-right shunt at this level is prevented by the closure of the foramen ovale. However, if a considerable atrial septal defect is present, the two ventricles fill from a common source, and what complement of blood each receives depends on the resistance to filling which each offers.

Thus, at birth, the heart size in such a situation is normal, and it is rare for a patient whose sole malformation is an atrial septal defect to die in the first year of life. At birth, moreover, the right and left ventricles are of about equal muscular development and the pressures in the systemic and pulmonary circuits are about equal. As time goes by, however, there is a fall in pulmonary vascular resistance and a rise in systemic resistance. Concomitantly, the muscular development of the left ventricle comes to exceed that of the right, and the resistance to ventricular filling likewise becomes greater on the left side. Thus, it is easy to understand the gradual increase in the left-to-right shunt through the atrial septal defect as the resistance to passage of blood into right ventricle and pulmonary circuit becomes significantly less than that into left ventricle and aorta. This change occurs relatively slowly during the first year of life and the circulation is able to adapt itself to the derangement of hemodynamic pattern. The right ventricle and pulmonary artery pressures fall, and the normal regression of the fetal pulmonary vascular pattern takes place.

Accordingly, the patient with an atrial septal defect usually does very well in the first year of life, and rarely is the diagnosis made at this time. A further factor that may operate in this period is that, as the right atrium dilates, the atrial septal defect probably increases in size, further augmenting the left-to-right flow. Thus, most patients with this lesion have little in the way of symptoms during the first decade, and often the second as well. Frequently, however, they begin to note the development of symptoms in the third decade of life, consisting of insidious fatigue and dyspnea on exertion. The progression of the average case from this point onward can, so it seems, proceed along two paths.

First, a large pulmonary blood flow may be maintained, with a large left-to-right shunt at the atrial level and a low pulmonary vascular resistance. What rise there is in pulmonary artery pressure is on the basis of a large flow. Extreme dilatation of the right heart occurs, tricuspid valve insufficiency supervenes, and congestive heart failure with its typical features and sequelae may ensue, even in the presence of greatly increased right ventricular stroke volume and pulmonary blood flow.

Second, and more commonly, the natural history of the anomaly is governed by the development of obliterative disease in the pulmonary vascular bed, due perhaps to autochthonous thrombosis or miliary embolization associated with reversible and later irreversible arterial changes.

With the rise of pulmonary artery pressure that accompanies these changes, there is increasing hypertrophy of the right ventricle and increasing resistance to emptying of the right atrium. The left-to-right shunt at the atrial level diminishes in magnitude and may become balanced or reversed. The right ventricle eventually fails under the stress of the pressure load against which it must work—as against the more easily borne volume load of the patient whose pulmonary resistance remains low.

It must be emphasized that all combinations of these two types of process may be seen, and at all ages. The youngest patient in our series was operated on at the age of 10 months. We have seen patients in their seventh decade who still had a high pulmonary flow and a low resistance. We have seen patients under 10 years of age who had severe pulmonary vascular changes and a balanced or reversed shunt. Finally, we have seen patients pass in a few years from the first group to the second in a period as short as a year or two.

It is with a background of this knowledge of the pathology and natural history of the disease that each patient is assessed, and only thus can the indications for surgery be clearly formulated.

INDICATIONS FOR SURGERY AND SELECTION OF PATIENTS

Early in the experience of this center, when the surgical risk was higher and complete cure in doubt, and with the knowledge that the defect is relatively benign as compared with other congenital heart defects, there was a natural hesitancy in advising operation. However, this had changed. Our confidence has increased as it has become increasingly apparent that this is a low risk operation—there has not been one operative death in the last 57 patients. Furthermore, postoperative catheterization data have shown that the procedure is curative, and observation of the patients after surgery reveals what benefits can come to them. While the outlook is on the whole relatively good for a patient with an atrial septal defect, it is nevertheless still true that the mean life expectancy is not much over 37 or 38 years. We know, too, that when trouble comes along, it may cause rapid deterioration, and we cannot predict exactly which patient will be thus affected. Therefore, at present, the diagnosis of the uncomplicated lesion in patients under 40 years of age is sufficient to be a firm indication for its surgical correction. Even in the very young age groups, surgery is strongly advised even though the patient is entirely asymptomatic. We believe that if an atrial septal defect is obliterated below the age of 8 years, the patient has an excellent chance of having a normal cardiovascular system by the time he grows into adulthood.

It is also considered that what risk is present is less in the younger age groups; we have had only one death below the age of 18 years in a patient with an uncomplicated defect.

The real decision, then, is when not to advise surgery, and this can, at times, be very difficult. The obvious patient to whom surgery must be denied is the one whose pulmonary resistance is so high that the interatrial shunt is balanced or reversed. The value of surgery lies in closing the defect and abolishing the increased pulmonary blood flow. In such a patient, surgery does not help and the operative risk is high. In general, it is true to say that with increasing pulmonary vascular resistance the benefits derived from surgery decrease while the risk of surgery increases commensurately. Where precisely the dividing line should be drawn is not easy to decide. However, in these c with a high pulmonary vascular resistance, a pulmonary blood flow of no more than one liter higher than the systemic should raise serious doubts as to the advisability of surgery.

Preoperative Assessment.—The diagnosis of an atrial septal defect is based upon careful clinical evaluation of the patient. Earlier in this unit's experience, the help provided by cardiac catheterization was also called upon to provide confirmation of the diagnosis, and to provide a series of values with which the postoperative results could be compared. Nowadays, it is believed that the diagnosis can be accurately established clinically in 90 per cent of cases, except in the evaluation of the presence or absence of anomalous pulmonary venous connections. However, these can be recognized and dealt with so expediently at surgery that this does not prove a serious practical problem.

The clinical assessment encompasses history, physical examination and consideration of the electrocardiographic and radiologic features. Much has been written about these, and therefore they will be mentioned only briefly, with details of the findings in this series. It must be stressed that, despite the broad limits imposed, this remains a group of patients selected for their surgical suitability.

History: The symptoms varied from none at all to marked incapacity. The most obvious were dyspnea and fatigue, these being present in like measure. Before surgery, 38 patients were essentially asymptomatic, 29 had mild, 23 moderate, and 10 severe disability.

Orthopnea was present before surgery in 5 cases.

Palpitation, expressed as such or as "pounding in the chest," was a not uncommon symptom, being experienced by 24 patients.

Chest pain was prominent in the histories of 10 patients, but only in 3 of these was it suggestive of coronary insufficiency.

A story compatible with congestive cardiac failure had been given in 7 cases.

Pulmonary infections had been prevalent in 31 of the 100 patients. Of these, 9 had had pneumonia in early life, while 7 had grown out of this predilection after the first few years.

Cyanosis on exertion was questioned in 6 cases on historical grounds.

Syncope, particularly on exertion, was prominent in the stories of 12 patients.

Physical examination: Most of the patients were underweight with respect to their height, and some (but by no means all) were undoubtedly of the asthenic or "gracile" habitus. A precordial bulging was present in 40 patients. The venous pressure was not usually elevated, although in the children with a very active heart, it was sometimes as high as 2 to 3 cm. above the sternal angle, a level we did not consider abnormal. A systolic thrill in the "pulmonary area" was observed in 7 cases. The precordium was always hyperdynamic in the region of the left lower sternal edge, and the lift of pulmonary artery expansion was usually felt. The shock of closure of the pulmonary valve was frequently appreciable. On auscultation, the classical systolic murmur caused by the passage of large volumes of blood through the pulmonary valve was heard in every case, maximally in either the second or third left intercostal space. A short diastolic murmur, heard either at the left lower sternal edge or more toward the apical region, was audible in 51 cases. This was considered to be due to increased volume of flow through the tricuspid valve. In no case, in the final analysis, was the diagnosis of "Lutembacher's syndrome" (i.e., atrial septal defect plus mitral stenosis) seriously entertained, and in no case was it found.

In 10 patients, *the presence of a high-pitched blowing systolic murmur* was detected along the lower left sternal border, and was considered to reflect tricuspid insufficiency. The murmur of pulmonary insufficiency was heard in 5 cases.

The second sound at the base of the heart was, in all cases except those with a high pulmonary vascular resistance, widely split and fixed with respect to the respiratory cycle. In the exceptional case with pulmonary hypertension due to increased resistance, the split was narrow or single, and the pulmonary element of the second sound loud.

The electrocardiogram: In no case was this normal. The degree of departure from normality was related to the extent of right-sided hypertrophy, this being interpreted, according to the findings, as reflecting hypertrophy of the right ventricle itself (RVH), its outflow tract (RVOH), or the region of the crista supraventricularis (CRISTA), the latter being the mildest form of abnormality. Though to some extent undoubtedly arbitrary, this classification has been found useful in comparing pre- and postoperative findings, and in relating the changes to the hemodynamic and anatomic findings. This subject will be thoroughly discussed in a subsequent publication.

RVH was present before surgery in 53 cases, RVOH in 44, and CRISTA in 3. The electrocardiogram showed the classical "partial right bundle branch block" pattern in most cases, although when the right ventricular hypertrophy was severe a qR *pattern* appeared in the right precordial leads. Some of the patients revealed the pattern of so-called "complete right bundle branch block" but we have been able to see no particular virtue in fixing an arbitrary limit for the QRS duration which separates a partial from a complete block.

Fluoroscopy and x-ray: Fluoroscopy was of the greatest help in the diagnosis. The heart was invariably enlarged, this being due to increased size of the right atrium and ventricle. The pulmonary arteries were large and pulsatile, and the vascular markings of the lungs exaggerated. The over-all activity of the heart was seen to be increased, the exaggerated excursion of the cardiac border being due to the increased stroke-volume of the right ventricle. The left atrium, left ventricle, and aorta were never prominent in the patient with an uncomplicated defect. In the 2 patients with an additional patent ductus arteriosus, however, the aorta was thought to be more conspicuous than usual.

Cardiac catheterization: Cardiac catheterization was performed prior to surgery in 93 cases, mostly at this center but also at various others where evaluation had been carried out before referral here.

The ratio of pulmonary index: *systemic index was greater than* 2.0 in 83 of the catheterized patients, and between 1.5 and 2.0 in 10. The total pulmonary vascular resistance, expressed as dynes-sec.-cm.$^{-5}$/M.^{2} exceeded 800 in 3 cases, the values being 910, 1,080, and 1,530, respectively.

Slight arterial unsaturation, less than 92 per cent, was found in 26 patients, but all of these had appreciable left-to-right shunts at the atrial level, and the oxygen level usually reflected mixing of blood in the two atria rather than a right-to-left shunt due to hypertension of the lesser circuit.

Anomalous pulmonary venous connections were found at catheterization in 8 patients.

Summary of preoperative diagnosis: On the basis of the procedures outlined above, 100 patients were selected for surgery with the diagnosis of atrial septal defect, secundum variety. Two were considered to have in addition a patent ductus arteriosus, and 8 to have anomalous pulmonary venous connections in addition to the atrial septal defect. In no case was the diagnosis of Lutembacher's syndrome made, and in no case was an ostium primum or atrioventricularis communis lesion suspected. Moreover, in no patient not included in this series was a diagnosis of septum secundum defect made when a septum primum or atrioventricularis communis defect was actually found at surgery.

HYPOTHERMIA

The growth and development of the use of hypothermia in this clinic have been the subject of many communications. As we have matured in the management of this modality with increasing experience, we have stablized our technique to include several specific procedures and precautions. When used within these limitations, it is our opinion that circulatory occlusion during hypothermia per se is a procedure essentially without risk; that is to say, considerably less than 1 per cent. Since, in our hands, this is considerably safer than other open-heart techniques for short procedures, we have continued to use the method despite the ready availability of cardiopulmonary bypass.

These general precautions in the use of hypothermia may be summarized as follows.

1. The range of the lowest rectal temperature achieved is 30° to 32° C. Circulatory arrest is performed at this temperature. This limitation in degree of hypothermia is extremely important.

2. Cooling is accomplished simply by immersion in ice water. There appears to be some rationale in cooling the peripheral tissue ahead of the heart and other vital organs.

3. Throughout the entire procedure, a deliberate respiratory alkalosis is maintained by hyperventilation.

4. Throughout the course of the cooling, operation, and warming, dextrose is administered intravenously. Evidence is increasing that intravenous nutrients have a beneficial effect on the myocardium in hypothermia.[40]

5. The first two units of blood used *during operation* are heparinized, having been freshly drawn in plastic bags. The presence of platelets, fibrinogen,

and other enzyme elements of the clotting mechanism, together with the absence of citrate, are considered helpful in avoiding the bleeding diathesis of hypothermia Transfusion is given freely because a low blood volume is poorly tolerated in hypothermia [11]

6 A bilateral sternum splitting incision is always used in order to achieve adequate exposure and allow proper positioning

7 Great care is taken to position the patient so that the cardiotomy is in the uppermost portion of the heart, thus materially reducing the risk of air embolism occurring in the coronary arteries

8 After the establishment of inflow occlusion to the heart the coronary circulation is perfused with 1 to 2 c c of 1 4 000 neostigmine in order to slow the heart The decreased metabolic needs of the slowly beating heart apparently are important in reducing the risk of ventricular fibrillation

9 The root of the aorta is always clamped to prevent coronary blood flow during occlusion This helps avert coronary air embolism, maintains bradycardia, and diminishes the coronary return to the heart, thus ensuring a dry operative field

10 The period of circulatory arrest must not exceed 6 minutes If more time is needed to complete the procedure, the operation should be interrupted and the circulation restored A second period of occlusion can then be instituted after an appropriate interval to complete the procedure The principle of multiple short occlusions allows at least 10 minutes of safe intracardiac time

11 Warming is achieved by diathermy, which is a form of internal warming There appears to be some rationale for rewarming vital internal organs before peripheral tissues

OPERATIVE TECHNIQUES

The chest is prepared for a bilateral, transsternal thoracotomy which is made in the fourth intercostal spaces, and which is carried across the sternum in a "V" fashion to permit a strong mortice closure A rib spreader is introduced at the level of the sternum and gradually opened as the suspensory ligaments of the pericardium are divided Meticulous hemostasis is observed

Visual and palpatory examination of the mediastinum and heart are conducted after the pericardium has been opened to confirm the preoperative diagnosis and to search for other attendant anomalies such as anomalous drainage of the veins of the right lung into the right atrium or superior vena cava, pulmonic stenosis, patent ductus arteriosus, and persistent, left superior vena cava In the latter event the hemazygos vein may join the left superior vena cava just before the junction of the latter with the coronary sinus (Fig 2, *d*) If steps are not taken to occlude both of these vessels during cardiotomy, an annoying amount of venous blood will continue to flow from the ostium of the coronary sinus and compromise the technical exposure

Umbilical tapes are passed about the superior and inferior vena cava intrapericardially To encircle the superior vena cava, the pericardial reflexion which binds it to the underlying right pulmonary artery must be divided carefully. The tape about the inferior vena cava should be placed as caudad as possible so that it will not interfere with the repair of the defect if it is associated with a prominent valve of the inferior vena cava.

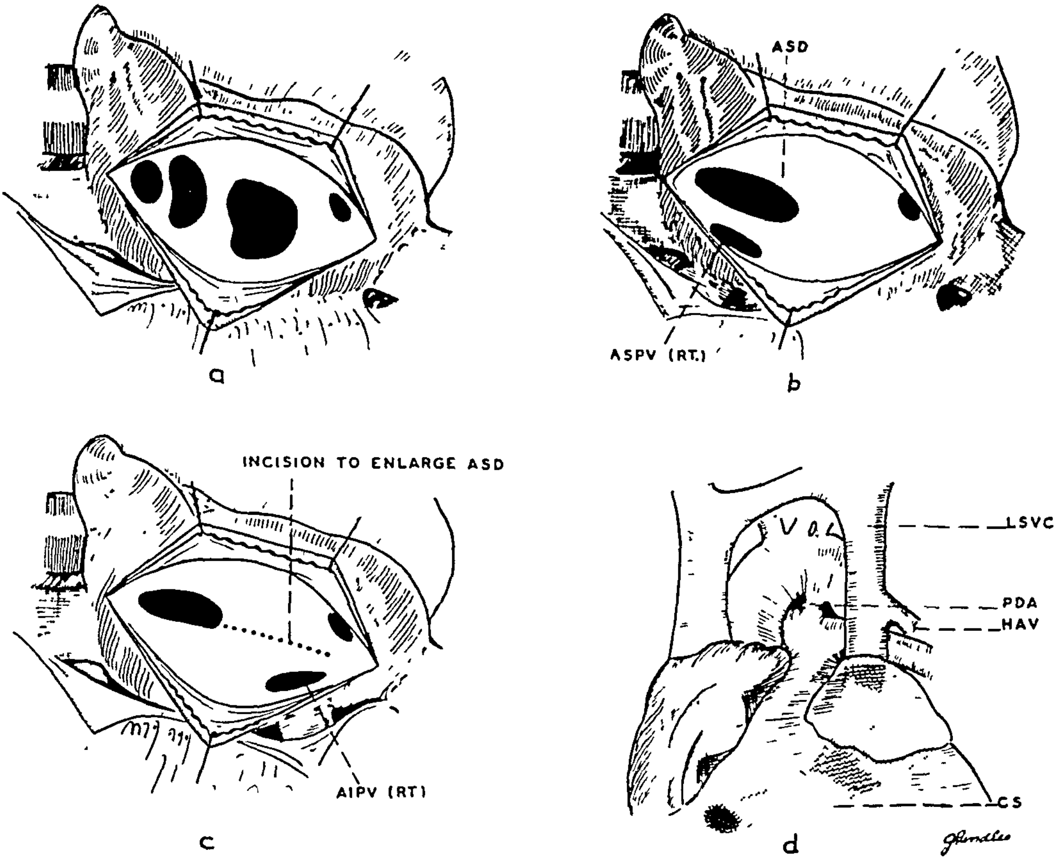


Fig. 2.—Some anatomic variations encountered in secundum defects.
a, Multiple openings involving both the foramen ovale and the septum secundum.
b, Septum secundum defect with anomalous right superior pulmonary vein.
c, Septum secundum defect with anomalous right inferior pulmonary vein.
d, Patent ductus arteriosus or left superior vena cava with hemiazygos vein may be present and should be carefully looked for before circulatory occlusion is attempted.

The wall of the right auricle is invaginated to permit palpation of the interatrial septum. In many patients we placed a purse-string suture on the right auricle tip and made a digital examination of the interior of the auricle. We found that our efficiency by this maneuver in describing precisely the pathology which was later seen through the open cardiotomy was only about 80 per cent. We missed some of the defects when they were multiple, some of the anomalous veins, and the relation of the inferior vena cava to the defect. Perhaps had we persisted we might have improved our sense of "feel," but since we found the procedure inaccurate and unnecessary we abandoned it.

Quadrant stay sutures of silk are now placed in the atrial wall overlying the defect to permit an atriotomy which will run diagonally from the inferior vena cava toward a point about midway between the superior vena cava and the right auricular tip. A noncrushing clamp is placed over the stay sutures and an atriotomy performed, about 5 cm. long. By tilting the patient to the left, and with the head of the table well elevated, the plane of the interatrial septum is brought into a horizontal position, and the atrial septal defect is placed in a superior position relative to the left ventricle and auricle. This maneuver we consider very important in the prevention of coronary air embolism.

The ligatures about the venae cavae are tightened and about 30 seconds allowed for cardiac emptying to occur. The aorta is occluded distal to the coronary ostia and 1.0 to 2.0 c.c. of 1:4,000 neostigmine (depending upon the size of the heart) is injected into the aortic root. Coronary perfusion of this parasympathomimetic drug is achieved by the cardiac contractions. The aortic clamp is removed and a right angle or oblique noncrushing clamp is introduced through the transverse pericardial sinus to occlude aortic and pulmonary artery flow. This clamp is placed against the very base of the aorta snugly to occlude the coronary ostia and discourage coronary air embolization.

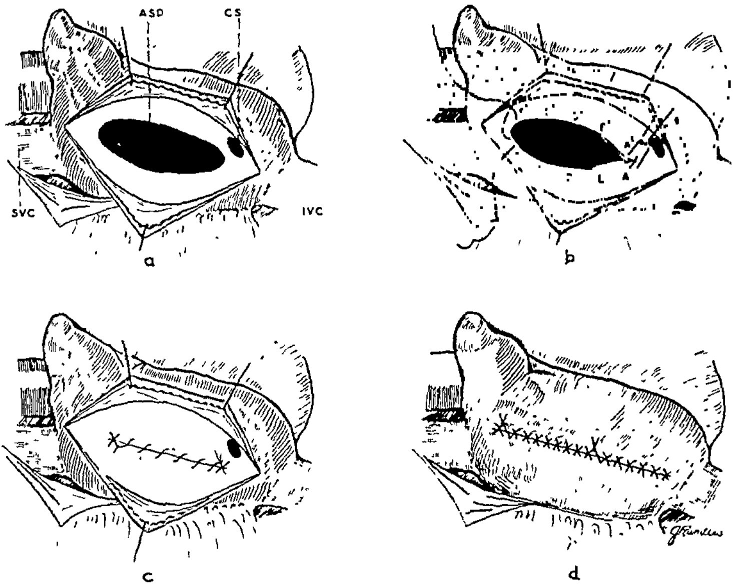


Fig 3.—The surgical steps taken in the closure of a typical simple defect of the foramen ovale type.

a, The relationship between the atrial septal defect *(ASD)* and the coronary sinus *(CS)* is shown.

b, A mattress suture has been placed at the lower end of the defect. This is tied before a similar suture is placed at the upper end. The closure will approximate *A* to A^1, *B* to B^1, etc.

c, The upper suture has been used as a continuous stitch and then tied to one end of the first (lower) mattress suture

d, The auricular wall is closed with continuous mattress sutures to enhance control of bleeding from the auricular wall arteries.

The atrial clamp is removed and the heart emptied by aspiration. Free of blood, the atria collapse, and the lips of the septal defect coapt. If the holes are multiple, they are converted to a single opening by excision of the thin partitions (Fig. 2, *a*). The locations of the tricuspid valve, coronary sinus, inferior vena cava, superior vena cava, and orifices of the pulmonary veins are ascertained. A finger is placed into the mitral valve, transseptally, to assure its adequacy. A figure-of-eight suture of 2-0 silk is placed in the most caudad aspect of the defect and held by an assistant. The ligature about the inferior vena cava is loosened momentarily so that a free flow of blood from its orifice will establish its relationship .to this first suture. A similar stitch is placed in the caphalad angle of the defect and run as a continuous suture caudad to be tied to the original suture. Prior to this final maneuver, the last few millimeters of the defect are permitted to gape while the right atrium is flooded with blood from the superior vena cava. In this way, residual air in the left atrium is allowed to escape as this chamber is filled with blood. The final tie is completed. The superior vena cava is released thus filling the right auricle. The atriotomy clamp is applied, and the clamp across the great vessels removed. The right coronary arteries are scrutinized for evidence of air emboli. (If emboli are noted, the aorta is clamped distal to the coronary ostia and manual, intermittent cardiac compression introduced immediately to propel the air distally.) Without such a complication, however, the vigor of the myocardial contraction slowly improves. The inferior vena cava tape is removed and cardiac action resumes its preocclusion characteristics. Interestingly, a transitory, systemic hypertension often occurs at this time.[42] Rewarming is begun.

The atriotomy is closed with a continuous mattress suture in order to occlude the atrial branches of the right coronary artery which, on two occasions before this suture was adopted, caused trouble by postoperative bleeding. Bilateral, posterior chest tubes are placed. The wound is closed in layers with steel wire sutures to the sternum and interrupted silk stitches to the muscular and fascial layers.

The total time of circulatory occlusion is now limited to 6 minutes; a period deemed safe on the basis of both laboratory and clinical experience. It has been impossible to close all of the defects in 6 minutes. In such circumstances, an additional period of occlusion has been used with intervening periods of normal flow lasting 10 to 20 minutes. Four patients have under gone multiple occlusion, all with good results.

One of the pitfalls in the repair of what appears to be a simple lesion is the failure to recognize the fact that the Eustachian valve of the inferior vena cava forms the lower margin of the defect. Closure of these enticing margins will transplant the vena cava to the left auricle, a fatal technical error. To reassure ourselves that the inferior vena cava is entering the right side of the inferior end of the suture line, we release for a moment the tape on this cava to observe directly the exact point of entry of this structure into the auricle. The maneuvers taken to correct this anomaly are illustrated in Fig. 4. Essentially, total excision of the valve itself is the primary maneuver. The lower stitch in the closure of the defect must now be placed high enough above the mouth of the cavae to allow free entry into the right auricle. Significant partial obstruction of the inferior cava is probably not tolerated by man any more readily than it is by the experimental animal.[43]

If anomalous drainage of a right pulmonary vein is associated with persistence of inferior vena cava valve, the repair will involve enlargement of the auricular defect in accordance with general principles to be described below. A final measure to avoid any possibility of vena cava pressure is to clean the epicardium from the auricular muscle at the point of entry of the vessel. In one instance, we felt it desirable to perform what was essentially a "pyloroplasty" at this point to enlarge the mouth of the cava toward the right.

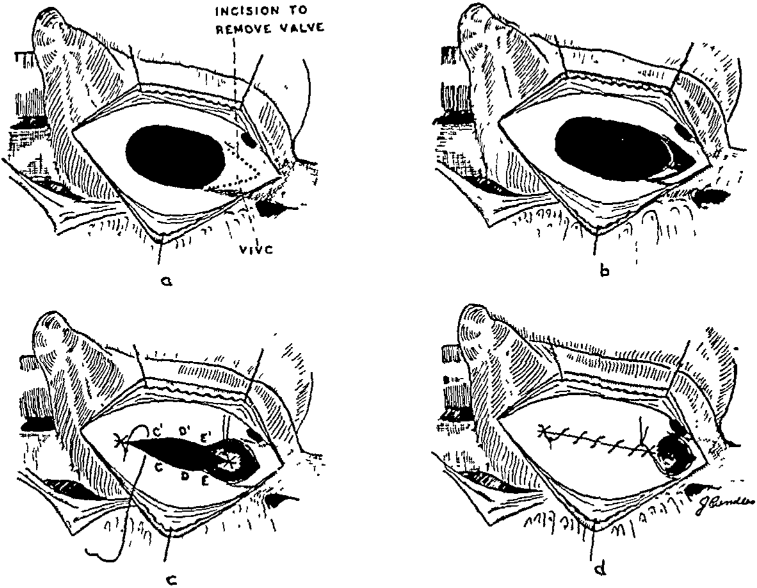


Fig. 4.—A false impression that the inferior border of the defect is the valve of the inferior vena cava *(VIVC)* can be easily held. Simple suture of this apparent defect is fatal, since the inferior vena cava will enter the left auricle. The steps in the repair are illustrated.

a, The valve of the inferior vena cava *(VIVC)* is excised along the dotted lines.

b, The true edges of the septal defect can now be seen.

c, The two mattress sutures have been carefully placed and the upper one is being run as a continuous stitch.

d, The completed closure leaves the inferior cava entering the right auricle.

As mentioned, 14 patients had anomalous pulmonary venous drainage from the right lung and one patient had anomalous return from the left via the coronary sinus. In every instance save one it was possible to devise an operative procedure which would redivert all the pulmonary blood into the left auricle and at the same time close the communication between the two auricles. In the remaining patient one small anomalous vein high on the vena cava remains untreated. This maneuver usually involves enlarging the atrial septal defect so that an opening is created through which the anomalous veins may drain freely to the left side without any obstruction. The effect of pulmonary venous obstruction has been previously described.[11] Such obstruction is highly undesirable, since the pleural adhesions which will form and through which will flow the pulmonary venous blood constitute a right-to-left (lung to thoracic wall venous system) shunt that will defeat the purpose of the operation. Every precaution must be taken, therefore, to avoid pulmonary venous congestion in these maneuvers. It is for this same reason that simple ligation of a single anomalous pulmonary vein entering high on the vena cava will result in no beneficial effect whatsoever. In this rare circumstance, if the vein cannot be safely transplanted, simple ligation of the pulmonary artery to the pulmonary segment is the procedure of choice, while the vein is not

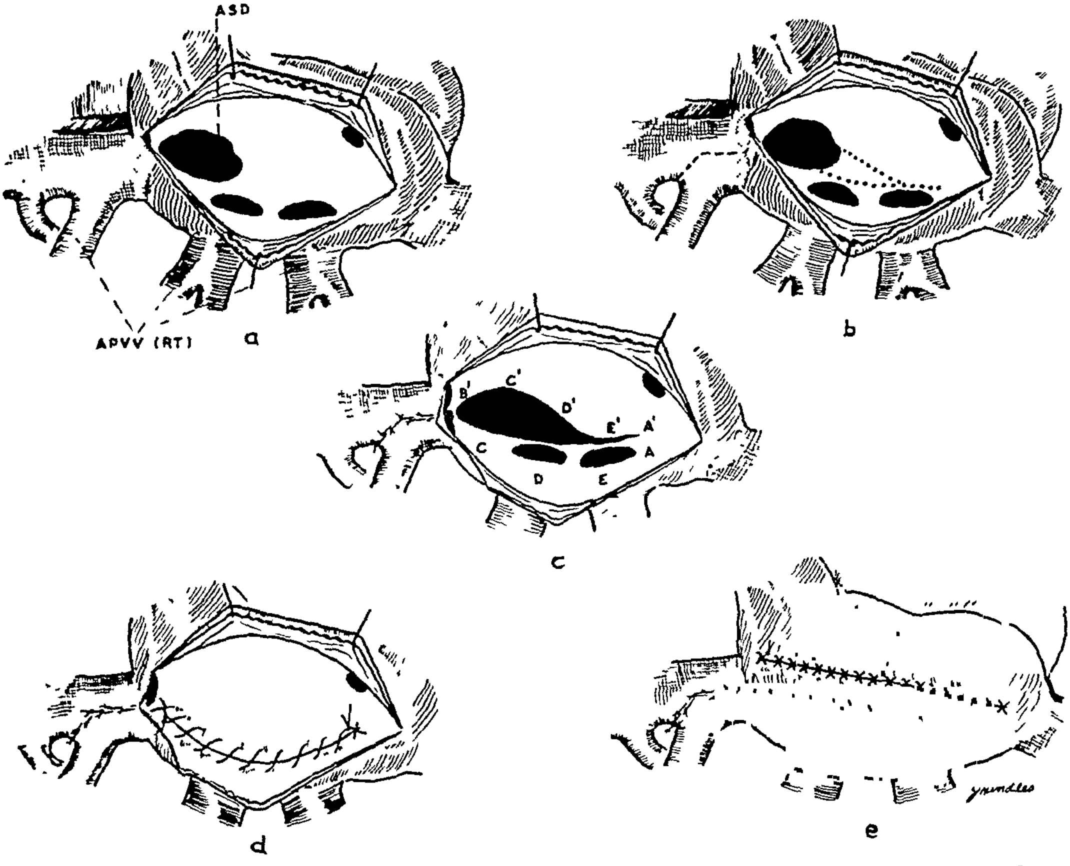


Fig. 5.—The surgical steps in the repair of a patient with defect of the septum secundum associated with total anomalous pulmonary venous drainage from the right lung are illustrated.

a, The most superior anomalous pulmonary vein enters the superior vena cava; two other right pulmonary veins enter the right auricle.

b, The first steps in the repair are shown. An interrupted suture line will be placed in the superior vena cava as indicated by the broken line, thus bringing pulmonary vein blood into the right auricle through a separate lumen which will be made to enter left auricle when the septal defect is closed. This defect must first be enlarged, however, by incisions along the dotted lines.

c, After placing the vena caval sutures from outside, the septum is opened and the proposed closure is indicated by the letters A—A^1, B—B^1, etc.

d, The completed suture line is shown. The lateral bites of each stitch are taken well up on the lateral wall of the right atrium, thus protecting against pulmonary venous congestion by enlarging the left auricle.

e, The completed operation is shown following auricular wall closure. The amount of right auricular wall used to enlarge left auricle is seen in the lower portion of the diagram.

molested. Thus, bronchial artery blood will nourish the lung and drain to the cava. If the operator desires to indulge in segmental resection, it will be curative but the risk will be greater.

When the highest pulmonary vein or veins enter the superior vena cava just above the right auricle and below the azygos vein, as is commonly the case, the maneuvers illustrated in Fig. 5 have proved satisfactory. The first critical consideration is the separation of the systemic from pulmonary venous flow within the vena cava by converting that structure into a double-barreled vessel. The pulmonary limb is made definitely adequate *even at the expense of what the operator would desire for the caval blood.* The azygos vein is carefully preserved in this procedure to provide a safety valve, and we have seen

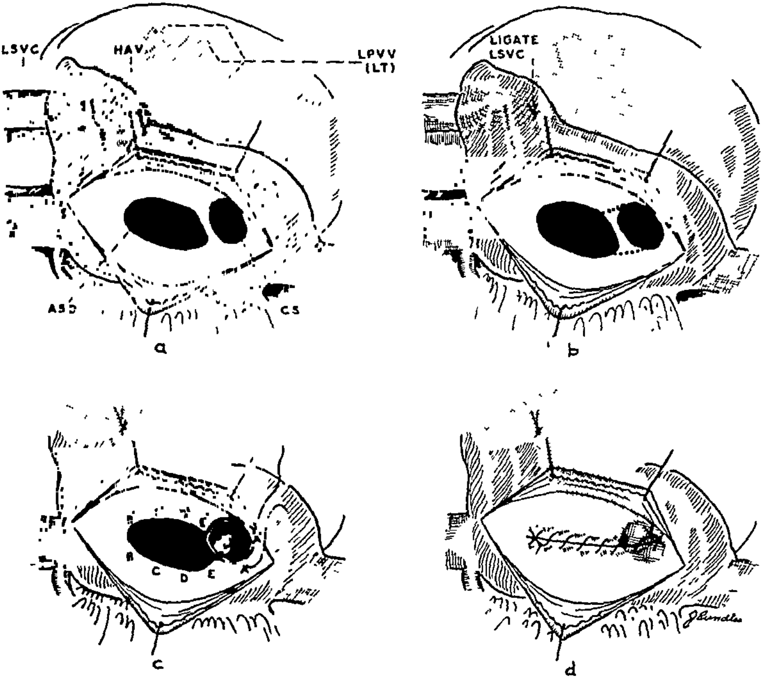


Fig. 6.—The steps taken to solve the problem of total left anomalous pulmonary venous drainage via the coronary sinus are illustrated.

a, The pertinent anatomy of the defects is diagrammatically presented. Note the persistent left superior vena cava *(LSVC)*, hemiazygos vein *(HAV)*, and the drainage of the left pulmonary veins *(LPVV)* into the coronary sinus.

b, The left superior vena cava has been ligated below the hemiazygos vein. The tissue separating the defect and the coronary sinus, together with the wall of the coronary sinus as it traverses the left auricle, will be excised

c, The coronary sinus will now be transplanted to the left of the closure when *A* is approximated to A^1, B to B^1, etc.

d, The closure has been completed. The entire pulmonary venous drainage the left auricle as does the blood from the coronary sinus.

no difficulty result from this procedure in these patients. This entire maneuver can be readily done from without, i.e., a closed maneuver, before the auricle is opened, by a row of mattress sutures placed along the side of a Potts clamp or even without such a clamp being used. The sutures are passed from in front of vena cava to the back and then redirected anteriorly, where they are tied.

The second consideration is the enlargement of the atrial septal defect so that the veins and the new limb of the superior vena cava may be transposed.

The final consideration is the deliberate use of a centimeter or more of right atrial wall to add to the left atrium. By coming anteriorly in this fashion and using some of the abundant right atrium, any tendency to squeeze the pulmonary veins by the septal closure is avoided. In effect, this maneuver moves the posterior attachment of the atrial septum to the right and anterior, thus enlarging the left atrium which is, of course, hemodynamically desirable.

One final, albeit rare, anatomical variant is illustrated in Fig. 6. The left pulmonary veins entered a left superior vena cava which drained into right auricle via the large coronary sinus. By enlarging the septal defect and excising the upper lip of the coronary sinus (Fig. 6), a single defect was created which could be readily closed by continuous suture. The flow through the coronary sinus now entered the left auricle. Following ligation of the left superior vena cava below the hemiazygos vein, this flow consisted of the entire venous drainage from the left lung and the coronary venous blood usually found in the coronary sinus. This small right-to-left shunt, however, is undetectable clinically, and the patient's course has been excellent. This patient's problem has been the subject of a separate report.[45]

REOPERATIONS

Four patients in this series were operated upon as second attempts to repair their defect. Three of these were patients on whom our original closed "button" techniques had been performed, but who were shown to harbor residual shunts. One of these (R.B.) was operated upon on June 4, 1952. The defect was partially closed, as we found at second operation, but hemodynamically, the shunt was still immense. The second was a young girl (*D.D.*) who had previously had a polyethylene button of considerable size fixed in position across the upper portion of her defect. She was much improved, but because of a large measured residual shunt, reoperation was performed. The button was found to be in excellent position occluding about 80 per cent of the defect. A crescent-shaped hole at the lower pole, however, remained. The button was left in place and the residual defect was closed by a series of sutures from rim to button. The third patient (W.G.) was similar to the second, and secondary repair was also successful.

The final patient (J.U.) was one in whom open operation had been performed. At the first procedure, he had a low lying defect, but one not technically difficult to close. Interrupted sutures were used. Recatheterization revealed him to be improved but not cured. A moderate shunt remained.

Accordingly, he was reoperated upon, and a slit like opening not over a centimeter long was seen between two of the previously placed sutures. This was easily closed and he has done well. As a result of this experience, we shifted to using a continuous suture to close the defect.

Our conclusions from this experience, therefore, may be summarized as follows: (1) Second bilateral thoracotomies during hypothermia are extremely difficult, and we think, hazardous. The many adhesions which tend to bleed profusely add technical difficulties and require extensive transfusion. The time to cure a patient of atrial septal defect is at the first operation. (2) Only one goal for the operation is acceptable, namely one hundred per cent closure of the defect. Eighty or ninety per cent closure is inadequate, since significant shunts will remain. (3) The desirability of open techniques where all defects can be seen and all anomalous veins transposed seems to us so obvious as no longer to need reiteration.

POSTOPERATIVE MANAGEMENT

Little is required in the postoperative care of these patients that is not observed following any thoracotomy. Blood loss from the chest tubes is replaced in equal volume. Narcotics are not administered until the patient is fully awake and his vital signs stable. Thereafter, narcotics or sedatives are given regularly every 3 to 4 hours, during the first day or 2 to diminish "splinting" of the chest due to pain. Venous pressure is assessed several times during the early postoperative period by direct measurement and also by observation of liver size and the height of jugular filling. Chest tubes are usually removed 24 hours after operation and ambulation begun. Myocardial failure is treated if and when it occurs. Prophylactic digitalization is not employed.

Adults with evidence of a large pulmonary vascular bed are placed on anticoagulant therapy as soon as the chest tubes are removed. Heparin followed by Coumadin is employed. The therapy, designed to prevent intravascular pulmonary thrombosis, is maintained for 2 to 4 weeks, or longer if indicated.

Bleeding tendencies, when they occur, are usually due to elevated titers of fibrinolysin, and are usually self limited. Specific therapy consists of administering fibrinogen alone or in company with fresh, whole, warm, citrated blood. For maximal benefit, fibrinogen should be given rather rapidly in order to saturate the fibrinolysin enzyme system. Calcium chloride, Premarin, Adrenosem, and protamine sulfate have been used at various times empirically.

Occasionally, diathermy burns occur, despite attempts to avoid them by placing felt pads between the diathermy coils and the patient, foam rubber pads under the hips, and by keeping the diathermy leads from touching towel clips, electrocardiogram leads, and thermocouple wires. The diathermy is used intermittently. Two minutes on, alternating with one minute off, is the safest effective technique we have found.

COMPLICATIONS AND MORTALITY

Certain of the operative and postoperative complications encountered in this group were of a type common to any major thoracic [illegible]

Others, however, were peculiar to the open-heart closure of congenital cardiac defects during hypothermia and, as such, stimulated our interest particularly. In this latter category may be included: ventricular fibrillation, coronary air embolization, bleeding dyscrasias, pulmonary vascular thrombosis, myocardial failure, peripheral neuropathy, and diathermy burns.

Ventricular fibrillation developed during the operative procedure 16 times in 12 patients. Of these, 11 patients were successfully defibrillated and are still living. The first patient to experience fibrillation was a young girl, early in our series, who was cooled to 23.2° C. Her ventricles fibrillated as she was transferred from the cooling tub to the operating table (mechanical trauma). Defibrillation was achieved with potassium chloride and the septal repair completed uneventfully. The remaining 11 hearts were defibrillated with electric shock, observing principles outlined previously.[16] Nine episodes of fibrillation occurred relatively spontaneously: one at the conclusion of cooling; one upon atriotomy; one upon closure of the septal defect; one during auricular closure; three upon resumption of circulation; and one each at 3 minutes and 4 minutes after resumption of circulation. No evidence of coronary air embolization was observed in any of these. Seven episodes developed in conjunction with some specific event. One during pre-occlusion manipulation, one during atrial closure in which the atrial clamp was seen to encroach upon the right coronary artery, one following the removal of padding from beneath the patient allowing the patient to fall to the table with a jar, and four were associated with air embolization of the right coronary artery. Almost all of the spontaneous fibrillations occurred when the body temperature was below 29° C. Since we have been using the range of 30 to 32° C., fibrillation has occurred only when coronary circulation has been obstructed by air embolization.

It has been our policy to place cylindrical pads in a "T" arrangement under each patient—the vertical pad under the right side of the horizontal pad which is in the mid-thoracic area. These serve to accentuate extension and to elevate the right shoulder and chest, thus aiding the exposure of the right auricle. During removal of these pads to facilitate thoracic closure, one of our patients dropped the intervening 2 or 3 inches to the operating table. This jolt served as sufficient stimulus to incite fibrillation. Electrical defibrillation was eventually achieved; but the resuscitation was arduous and the patient died suddenly 14 hours postoperatively, possibly from a terminal episode of ventricular fibrillation. Since this experience we have exercised utmost caution to protect the whole patient from any mechanical shock.

Air embolization of the right coronary artery was observed immediately after re-establishment of the circulation in 10 patients. In 4, this was followed by ventricular fibrillation, and in 6 no arrhythmia occurred. The uncomplicated outcome of these last 6 is due, we believe, to immediate vigorous steps taken to drive the air distally in the coronary circuit, i.e., cross-clamping of the ascending aorta distal to the coronary ostia, accompanied by firm, intermittent manual compression of the cardiac ventricles. The prevention of this complication depends on extremely careful attention to allowing all the air in the left heart to escape before the final stitch in the septal defect is tightened In complicated lesions, when time is running short, this maneuver may be performed too hurriedly to be effective

Bleeding of marked degree occurred postoperatively in 6 patients in whom its cause was not readily explained, i e, unrelated to bleeding from a specific vessel, or to anticoagulant therapy Of these, 2 died of the hemorrhage The operative temperatures ranged from 26 5° to 30 0° C in this small group The role played by temperature itself in the "bleeding diathesis" is uncertain, but since we have limited the temperatures to the range 30 0° to 33 0° C, bleeding has been no particular problem and has been associated with no fatalities Our general approach to the treatment of this problem was outlined earlier

As mentioned previously, we consider the possibility of pulmonary vascular thromboses a constant hazard in all adult patients with large left to right shunts Our reasoning is that such individuals have a pulmonary vascular system of greatly expanded volume This capacity remains more or less constant following closure of the defect, and, since the volume of pulmonary blood flow is much reduced, its velocity is correspondingly reduced This relative stasis is conducive to thromboses in these vessels as elsewhere Currently, all such patients are placed on anticoagulant therapy as soon as the chest tubes are removed Prior to the inauguration of this plan, six instances occurred in which pulmonary thrombosis was strongly suspected, 3 of these patients died The radiographic picture accompanying these changes is one of diffuse or scattered, progressive "bronchopneumonia" or "pulmonary infarction," and matches the pathologic changes previously demonstrated in the experimental animal[44]

Fatal thromboses in other vessels developed in 2 additional patients neither of whom was under anticoagulation therapy A 6 year old girl died 48 hours postoperatively of bilateral internal jugular vein thromboses It was thought that tight adhesive tape encircling the neck to hold in the endotracheal tub may have been an etiological factor in this patient A 21 year old female d veloped an occlusion of the left carotid artery on the third postoperative d and died on the sixth A 13 year old girl experienced an embolus to her a bifurcation on the fifth postoperative day which was successfully rem d These episodes raise the question of whether or not an excessive state of h per-coagulability occurs postoperatively in these patients That this may b so is strongly suggested by the studies of von Kaulla and Swan[47]

Myocardial failure was noted in 9 patients postoperatively all whom responded well to digitalis therapy All of these patients were over 10 years of age, and 5 of them were over 25 years

Two other complications are related to our method of inducing and relieving hypothermia Four patients experienced a transient neuropathy of hands or arms This was found by Stephens and Appleby[48] to be a injury of the nerves due to cold immersion Careful attention to pr prolonged immersion of the extremities in the ice water has prevented quent similar difficulties Diathermy burns occurred in 8 patients Fe in adults, were sacral Prevention is attempted by placing felt padd the patient and the diathermy coil and foam rubber under the other patients were burned on the extremities where electrocardiogram electrodes or intravenous needles came in contact with the diathermy cables. Prophylaxis in this regard is obvious, and has been largely successful.

In this series, 93 patients survived their surgery. All 7 deaths occurred in the first 43 operations; the last 57 have been performed without mortality. Analysis of the causes of the deaths in the first part of the series led to the adoption of precautions which may be playing a role in the apparent improvement in operative risk. These deaths were primarily caused by the following factors:

Ventricular fibrillation	1
Blood clotting disturbance	
a. Bleeding	2
b. Postoperative thrombosis	4

Many of the precautions currently practiced to avoid these lethal complications have been already mentioned, but for the sake of emphasis we repeat them here. Ventricular fibrillation is minimized by:

a. Temperature not below 30° C.
b. Continuous respiratory alkalosis.
c. Constant intravenous glucose infusion.
d. Neostigmine by coronary perfusion at the start of circulatory arrest.
e. Careful avoidance of trapping air in left heart.
f. Avoid clamping right coronary artery in noncrushing auricular clamp.
g. Avoid jarring the cold patient.
h. Selection of patients who do not have nonreversible pulmonary hypertension (resistance over 700 dynes).

Disturbances in clotting mechanism are minimized by:

a. Temperature not under 30° C.
b. Preoperative treatment of a depressed prothrombin time with vitamin K^1.
c. The use of fresh blood in siliconized bottles for the first two units used at surgery.
d. Avoidance of constrictions of the neck during anesthesia.
e. Careful endocardium-to-endocardium closure of the auricle.
f. Postoperative anticoagulation of all adult patients with very large pulmonary vascular beds.

RESULTS OF SURGERY

Of the 100 patients in the series, 92 are alive. Seven died as a result of surgery, and one patient, aged 39, died 8 weeks after surgery from a cerebellar hemorrhage. It does not appear that this latter event can be related to the surgery; the patient was under the management of her personal physician and was taking anticoagulants at the time.

Of the 92 patients, we have recent information on 91. One lady we have been unable to trace, but learn that some months ago she removed to California. Forty-nine have been seen recently at this center; all the others live at considerable distances from Denver, and we have relied on the combined reports from the patients, their parents, and their doctors (frequently accompanied by roentgenograms and cardiograms) for an accurate assessment of their condition.

The follow up is 5 years in 3 cases, 4 years in 7, 3 years in 17, 2 years in 21, one year in 31, and 6 months in 13 cases, respectively. We have therefore been able to observe the changes in symptoms, signs, electrocardiogram, and x-ray studies which come about as a result of closure of the defect.

SYMPTOMS

In order to gain an over all picture of what change takes place, we must not forget that the disease expresses itself not only in terms of the major symptoms such as dyspnea, fatigue, and effort intolerance, but obtrudes into every small background pattern that goes to compose a patient's life. We have heard patients express their improvement in the fact of waking up refreshed instead of tired from a night's sleep, of being able to enjoy a late show or a late meal, of being able to go into the mountains without fainting, and so on. However, for the purposes of comparison, we shall confine ourselves to the major and overt symptoms which are more directly an expression of cardiovascular dysfunction.

For the purposes of analysis, we have again separated the symptoms into three grades: mild (Grade I), moderate (Grade II), severe (Grade III), stipulating broadly the criteria by which we put any given patient into a particular group.

Dyspnea and Fatigue.—

Of the 10 patients who suffered severe (Grade III) disability prior to surgery, 6 are now asymptomatic, while 3 were surgical mortalities. Of the 23 cases moderately incapacitated (Grade II) before surgery, 15 are now without symptoms while 2 are dead. Of the remaining 6, 3 are improved. Of the mildly (Grade I) incapacitated group of 29 patients, 27 are symptom free, one has as much disability as before, while one died at operation.

Thirty eight patients were free from symptoms before surgery. Thirty seven are now well, while one died following operation. Thus, of the 100 patients who went to surgery, 85 are now leading normal lives without significant symptoms.

TABLE II. EFFECT OF SURGERY ON THE SYMPTOMATOLOGY ASSOCIATED WITH ATRIAL SEPTAL DEFECT

SEVERITY	PREOPERATIVE STATUS	POSTOPERATIVE STATUS				DEAD
		0	I	II	III	
0	38	37	—	—	—	1
I	29	27	1	—	—	1
II	23	15	3	3	—	2
III	10	6	—	—	—	4
Totals	100	85	4	3	0	8

The rate at which improvement takes place after surgery varies from patient to patient. Naturally in a series as large as this many different types of reaction to the new found health have been seen. A few patients have substituted "functional" symptoms for their previous organically engendered ones. Some improve rapidly after surgery, for example, one jockey, age 32, was racing again 3 weeks after surgery; another patient was seen by her proud medical attendants to climb to the top row of a football stadium without any difficulty within 2 weeks of surgery. Most patients are leading normal lives within 2 or 3 months of operation, although in some cases slow improvement continues for upward of 12 months. There is usually a gain in appetite, weight, and zest for life; and many patients who had no real complaints before surgery state that they have gained in strength and energy, and only in retrospect do they realize that they were limited before.

The "Postcardiac Surgery" Syndrome.—

Previously described as the "post-commissurotomy syndrome" or "post-valvotomy syndrome," this illness has appeared since operation in at least 15 patients in this series. In a further 6, it may have occurred in a mild form. It differs in no way from the "post-commissurotomy syndrome" which follows surgery of the mitral valve, and is characterized by fever, malaise, pleurisy, and pericarditis. It responds rapidly to the administration of steroids, and untreated lasts from 7 to 10 days before subsiding spontaneously. In one patient, it has recurred 5 times, although most of the patients have had only one attack. In 2 cases, the illness appeared 8 days after surgery; in one not until a year later. When adequately treated it is not a significant cause of disability.

Changes in Physical Signs.—

As soon as the immediate postoperative period is past, it becomes possible to assess what changes had occurred in the physical signs. First, with the reduction in the stroke-volume of the right ventricle, the whole precordium became quieter and its activity less. In every patient, the systolic thrill disappeared. Almost invariably, the systolic murmur in the "pulmonary area" was less loud; in a few cases it disappeared completely. The residual systolic murmur was probably due to the persistent relative narrowing of the pulmonary valve in relation to the marked dilatation of the pulmonary artery causing turbulence and eddies. Gradually, over the ensuing months, the systolic murmur diminishes in intensity. The preoperative diastolic murmurs which are due to increased flow disappear. The rare diastolic murmur due to pulmonary insufficiency persisted in 2 cases and disappeared in 3.

The characteristic wide and fixed splitting of the second heart sound at the base has persisted unchanged in a few cases, but more commonly the sounds appear to return to a normal pattern with respiratory variation in the degree of splitting.

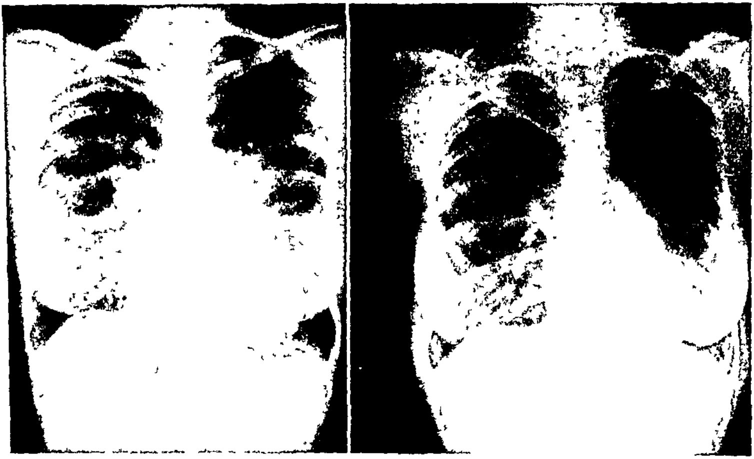
In summary, then, the changes which follow surgery consist of a diminution of precordial activity, disappearance of the systolic thrill, abolition or lessening of murmurs and, in most cases, a return toward normal second cardiac sound. This is, of course, usually accompanied by a diminution in heart size, and a gain in general physical well-being.

The electrocardiogram: We have had an opportunity to examine a recent electrocardiogram in almost all cases. When the defect has been closed, the tracing changes toward normal, the most characteristic feature being the diminution in the height of R′ (the secondary R wave) in the right precordial chest leads. In no case has this failed to occur except when the defect has not been obliterated (2 patients), or when irreversible pulmonary hypertension is present (one patient). If this change is not manifest within about 4 months, it is meet to look for the reason.

The subject of postoperative electrocardiographic changes will be fully considered elsewhere.

Fluoroscopy: At the first postoperative fluoroscopic examination, the previously hyperdynamic heart is seen to have become quiet, and the excursion of the cardiac border much less. The characteristic cardiac contour remains, however, and the pulmonary artery is still prominent, though far less actively pulsatile than before.

As time passes, there is usually a real diminution in cardiac size in the individuals whose heart was significantly enlarged preoperatively (Fig. 7). The bronchovascular markings in the lung fields also become less apparent as time passes. Again, therefore, there is a gradual continuing regression toward normal, although, in the case of the adults in whom significant cardiac enlargement was present before surgery, it is doubtful if the heart size and contour will ever return completely to normal.



A. *B.*

Fig. 7.—The regression in the pulmonary vascularity and in the size of the heart, which occurred in the 2½ years after surgery in this 23-year-old girl, is evident by comparing the preoperative *(A)* and postoperative *(B)* films.

Cardiac catheterization: This was performed after surgery in 44 cases. In 39 of these the results showed that the left-to-right shunt had been abolished. There were 5 cases in which there was evidence of a residual shunt at the atrial level. In 2 of these cases this is of significance; a boy of 12 who was operated on in 1954 using interrupted sutures, and a lady of 45, operated on in 1957, who had an extremely large heart and huge defect. In the other 3 cases, normal postoperative improvement has occurred, both objectively and subjectively.

The results of postoperative catheterization showed clearly that the preoperative elevation of pulmonary artery pressure was in *many* cases due to the high flow, and that as soon as this was reduced the pressure fell. Of the patients with a very high pulmonary vascular resistance (800 dynes-sec.-cm.$^{-5}$/M.^{2}) only one survived. She has recently been recatheterized, and the results show that there has been no regression in the severe pulmonary hypertension. Thus, on the basis of the objective evidence obtained by postoperative catheterization of almost half of these patients, the operation has been proved to be curative in the great majority.

SUMMARY

1. One hundred consecutive cases of atrial septal defect secundum seen at open-heart surgery have been analyzed and the data presented.

2. There were 7 operative deaths among the first 43 patients, none among the last 57.

3. The natural history of the disease, diagnostic criteria, and indications for surgery are discussed. It is urged that in the light of the safety of the operative procedure described, all patients with this diagnosis should be given the benefit of surgical repair unless the pulmonary resistance is greatly elevated.

4. The operative techniques employed to meet the various anatomic variations encountered are described. It is felt that hypothermia at the present time is the method of choice for the performance of these procedures.

5. The current status of all but one of the surviving patients is known and the data are analyzed. Eighty-one patients are symptom free and apparently cured by all means of assessment; 3 are improved but still have some symptoms; 3 have small residual shunts which do not seem to be of hemodynamic significance; one patient has become centrally cyanosed owing to the passage of inferior vena caval blood into the left atrium; one patient has persistent pulmonary hypertension after closure of the defect; 2 patients have residual shunts of sufficient degree to warrant re-intervention.

6. Atrial septal defect secundum is a congenital malformation which can be diagnosed clinically with great accuracy and which can be successfully treated surgically by open operation during hypothermia at a very low risk. Operation should be performed on essentially all patients with this disease during childhood, as soon as convenient after the diagnosis is made.

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THE ANATOMY OF ESOPHAGEAL HIATUS OF THE DIAPHRAGM AND THE PATHOGENESIS OF HIATUS HERNIATION

Paul Marchand, M.D., Ch.M., F.R.C.S., Johannesburg, South Africa

DIAPHRAGMATIC hernias are not uncommon. From January, 1952, to January, 1957, our unit dealt with 142 cases of which 119 (80 per cent) were hiatus hernias (Table I). An investigation has been undertaken to determine the reasons for the susceptibilty of the esophageal hiatus to herniation. The results of the anatomic studies are described here; they largely confirm the findings of Allison,[1] and of Collis, Kelly, and Wiley.[5]

Thirty adult diaphragms have been dissected. Fifteen specimens were removed from fresh cadavers after the crural origins had been displayed and were then fixed to a wooden board and preserved in 10 per cent formalin. Fifteen were dissected in situ on embalmed bodies in the anatomy hall.

TABLE I. LIST OF CASES OF DIAPHRAGMATIC HERNA TREATED IN ONE UNIT OF THE DEPARTMENT OF THORACIC SURGERY, JOHANNESBURG AND BARAGWANATH HOSPITALS OVER A 5-YEAR PERIOD*

A. *Traumatic Diaphragmatic Hernia*		12
*Following penetrating wounds	4	
Following crush injuries	5	
Following operative trauma	3	
B. *Congenital Diaphragmatic Hernia*		18
Persistent pleuroperitoneal hiatus (Bochdalek)	3	
Congenital absence of posterolateral part of diaphragm	3	
Total absen [illegible]	1	
Congenital [illegible]	2	
Parasternal [illegible]	2	
Aorta-esophageal hernia	1	
Infantile hiatus hernia	6	
C. *Acquired Hiatus Hernia*		112
Adult type (sliding and rolling)	110	
Acquired short esophagus (caustic stricture scleroderma)	2	

*Excluding acute penetrating thoraco-abdominal wounds

THE CRURA

In 1907, Low published his classical account of the anatomy of the diaphragmatic crura. He considered that the esophageal hiatus was "formed by

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From the Department of Thoracic Surgery, Johannesburg General Hospital.

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a splitting of the fibres of the right crus." This is an oversimplified description, as Collis, Kelly, and Wiley have shown.

The crura arise from one or more tendons whose fibers blend strongly with the anterior longitudinal ligament over the upper lumbar vertebrae. The left crus is usually attached to two lumbar vertebrae and the right to three, but they may arise at the same level from a common tendinous origin. Accessory tendons may arise from the fascia over the psoas muscles and from the medial arcuate ligaments but, though they form part of the crura, the fibers from these slips eventually fan out laterally to insert into the central tendon away from the hiatal limbs. The crura pass upward in close contact with the vertebral bodies for most of their course and only incline forward as they arch in front of the esophagus.

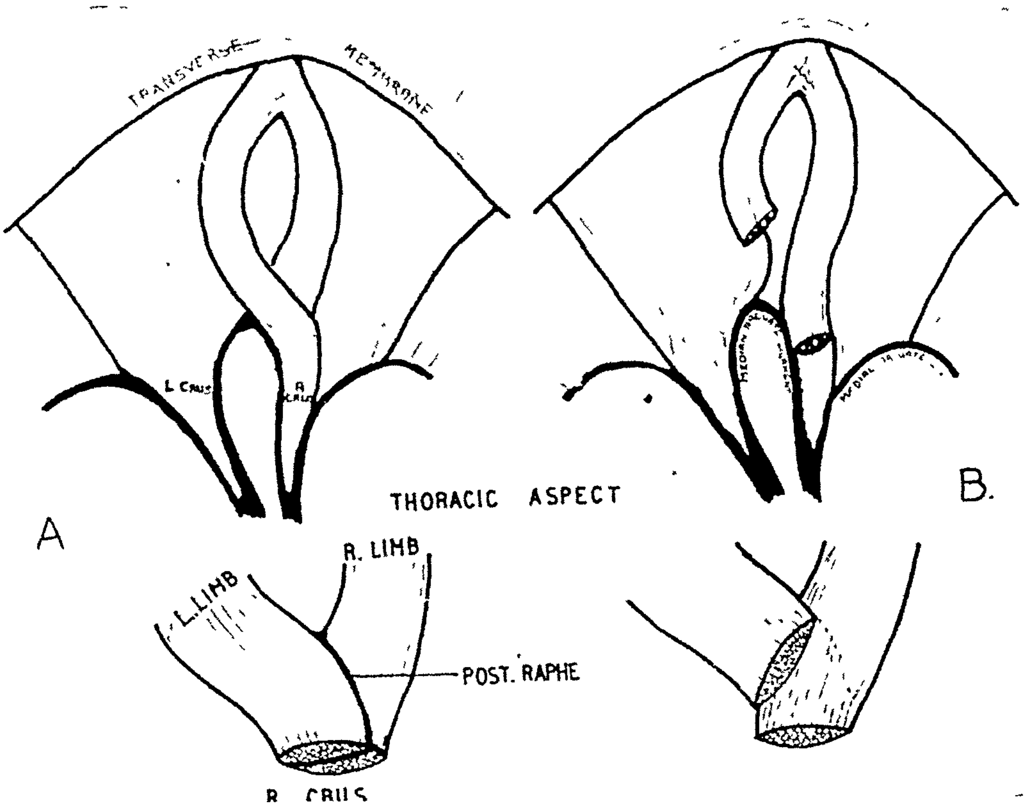

Fig. 1.—Illustration of the mode of formation of the hiatus. Two flattened muscle bands appear within the right crus separated by a plane of areolar tissue. The dorsal band forms the left hiatal muscle and the ventral forms the right hiatal muscle.

A, Muscle bundles intact. *B*, Segment of left (dorsal) limb of right crus removed to display the course of the right (abdominal) limb of the right crus. (*From* Marchand: Thorax 12: 189-202, 1957.)

As soon as muscle fibers appear within the right crus, they group themselves into two ribbonlike bands separated from each other by loose connective tissue. One bundle is dorsally placed (thoracic aspect) and the other ventrally placed (abdominal aspect). The dorsal band forms the left limb of the right crus and the ventral the right limb of the right crus (Fig. 1). The muscle bands soon diverge and cross each other in a scissorlike fashion, the ventral bundle passing upward and to the right, and the dorsal bundle passing upward and to the left. The laterally placed fibers of each hiatal limb insert directly into the central tendon of the diaphragm but the medial fibers, which form the hiatal margins, incline toward the midline in front of the esophagus and decussate in a trellis-like fashion with fibers of the opposite limb (Fig. 2). Although there are many variations of this standard pattern, all embrace the basic principle of early grouping of flattened muscle bundles which diverge in a scissorlike fashion.

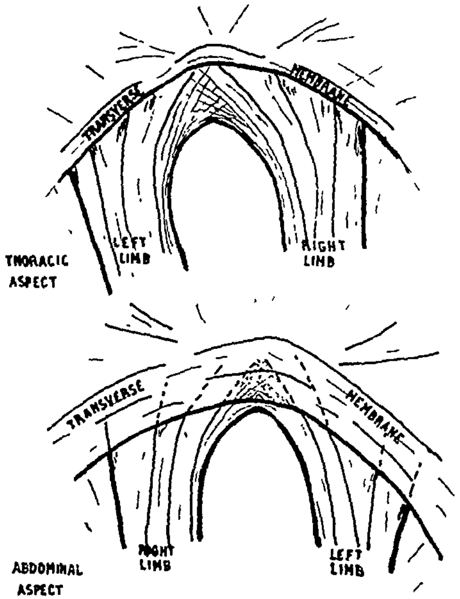

Fig. 2.—Diagram of the anterior edge of the hiatus illustrating the mode of insertion of the muscle fibers into the central tendon of the diaphragm. The medial fibers within each hiatal limb interlace with each other across the midline before inserting into the central tendon of the diaphragm. The transverse membrane of the central tendon supports the anterior decussating muscle fibers from the abdominal side. (*From* Marchand: Thorax, 12: 189-202, 1957.)

The Hiatal Orifice.—The hiatal orifice is elliptical in shape and its long axis lies in the sagittal plane. Sweet[20] and Harrington[9] have stated that the long axis lies transversely, but I agree with Allison[2] and Lam and Kenney[10] that this is not found in the normal body.

The elliptical shape arises naturally from the mode of origin and insertion of the hiatal muscles and the direction of their fibers. Any tendency toward widening of the transverse diameter is opposed by the crossover of the crural limbs and by the anterior decussating muscle fibers (Fig. 3).

Normally, about a centimeter of muscle separates the anterior rim of the hiatus from the central tendon of the diaphragm (Fig. 4). Lam and Kenney state that the anterior margin of the hiatus is formed by the unyielding tendinous tissue of the middle leaflet of the central tendon, but this I have seen only when a hiatus hernia is present. On the abdominal aspect, a band of transverse tendinous fibers underlies the anterior decussating muscles and this may verge on the hiatal orifice. This transverse ligament is a strong fibrous band which reinforces the posterior edge of the central tendon of the diaphragm. It is about a centimeter in width and is best developed on the undersurface of the diaphragm where it forms a sharp falciform rim to the anterior edge of the hiatus. Here it supports the decussating anterior muscle fibers and resists any force exerted from the direction of the esophageal hiatus.

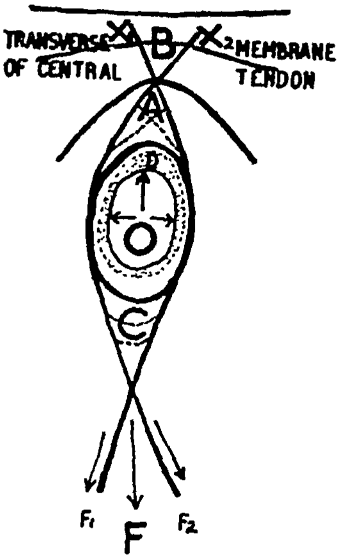

Fig. 3.—Diagrammatic illustration of the forces which tend to widen the esophageal hiatus and of the anatomic structures which oppose such disruption.

The disrupting force (*O*) is the intraperitoneal pressure which constantly tends to force the cardia through the hiatus and so widen the opening. This force is resisted by the construction of the hiatal mechanism.

F, Line of force exerted by the direction of pull of the hiatal muscles X_{1-2} – F_{1-2}.

A, Action of the anterior decussating muscle fibers which tether the anterior extremities of the hiatal limbs.

B, Transverse membrane which supports the anterior muscle fibers and so buffers the force of the intraperitoneal pressure.

C, Posterior intertendinous muscle (Fig. 7). These fibers tether the hiatal muscles behind the hiatus.

D, Esophagophrenic ligament which acts as an elastic anchor to the terminal esophagus within the hiatal canal.

THE RELATION OF THE ESOPHAGUS TO THE HIATUS

Under normal conditions the stomach cannot be displaced into the mediastinum. The restraining structures are the phrenoesophageal ligaments (described by Schatzki,[18] Anders and Bahrmann,[3] and Roux[17]) and an aggregation of posterior structures which include the vagus nerve and radicles of the left gastric vein and artery.[1]

The phrenoesophageal ligament is a definite structure. It is best developed where the terminal esophagus traverses the hiatus, extending for about a centimeter above the gastroesophageal junction. Above diaphragm level it thins rapidly and merges with the perivisceral fascia of the esophagus.[12] Below, the ligament reflects circumferentially to become continuous with the fascia transversalis on the undersurface of the diaphragm. If a finger is introduced into the lumen of the lower esophagus, the anterior reflection of the phrenoesophageal ligament is felt as a thick cordlike structure. This ligament is readily definable in the young but is less obvious in elderly people and is attentuated and inconspicuous when a hiatus hernia is present.

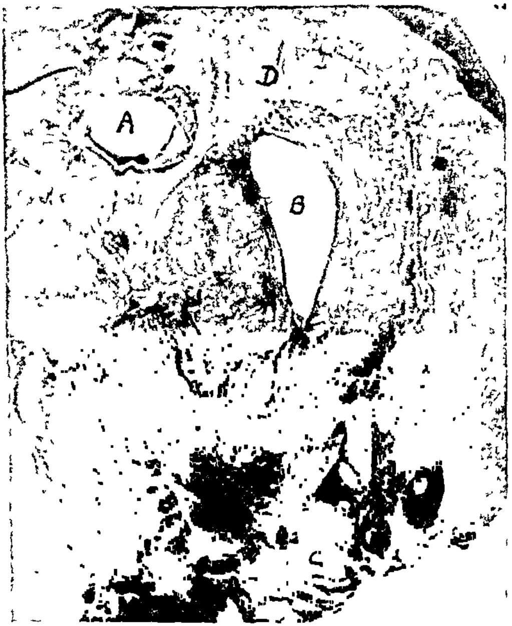

Fig 4—Dissection of a diaphragm of standard anatomic pattern viewed from below The elliptical shape of the hiatus is shown Note that the anterior margin of the hiatus is separated from the transverse ligament of the central tendon by muscle. (See text)

A, Inferior vena cava. *B*, Esophageal hiatus *C*, Aorta *D*, Transverse membrane of central tendon of diaphragm.

THE HIATAL ANATOMY IN THE PRESENCE OF HERNIATION

Two diaphragms were dissected in people with hiatus hernias who died from unrelated causes Detailed notes have also been made of the anatomic findings at 58 operations for repair of hiatus hernia.

In the presence of a hernia, the esophageal hiatus usually abuts directly on the transverse membrane of the central tendon and the anterior hiatal muscles are absent or reduced to a few atrophic strands (Figs. 5, 6, and 7). The hiatus itself is no longer a sagittal slit, but a rounded opening whose transverse diameter

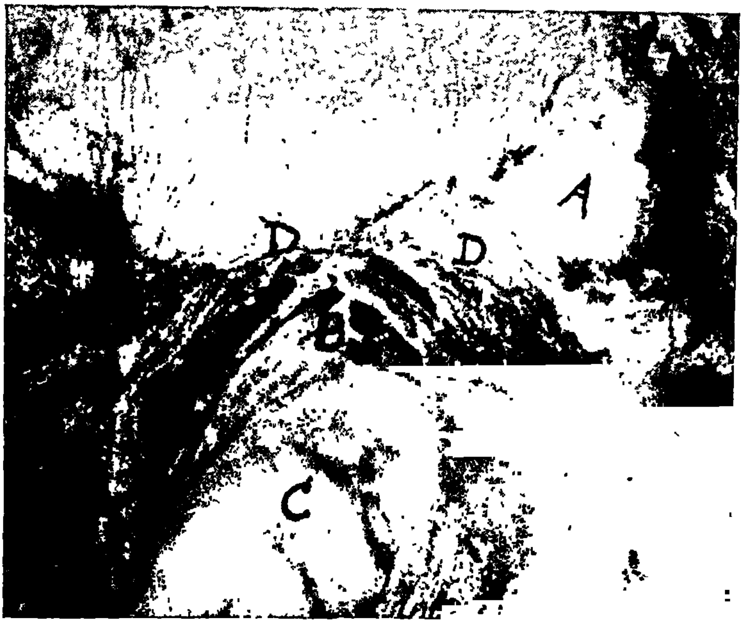

Fig. 5.—Dissection viewed from above of diaphragm which was the seat of a hiatus hernia. The hiatus abuts directly on the transverse membrane of the central tendon. The peritoneum herniating through the anterior defect was buttonholed in 2 places during dissection.

A, Inferior vena cava. *B*, Buttonholed peritoneal sac. *C*, Stomach herniated above the diaphragm. *D*, Transverse membrane of central tendon.

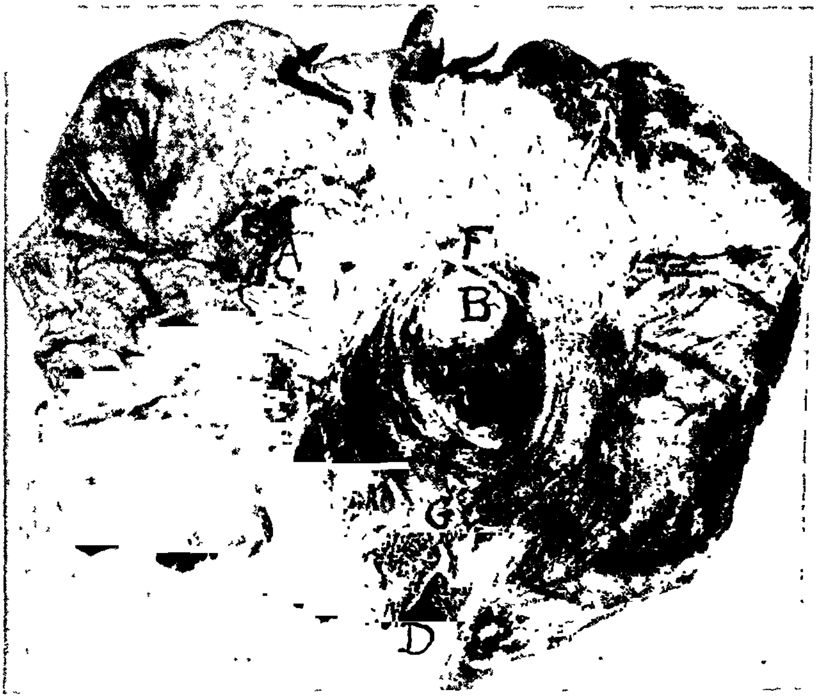

Fig. 6.—Dissection of a diaphragm associated with herniation of the stomach through the esophageal hiatus (viewed from below). The right hiatal limb is reinforced by a slip of muscle from the left crus; a post intercrural muscle is present. Note the rounded opening of the hiatus and the absence of muscle fibers lining the anterior rim of the opening.

A, Inferior vena cava. *B*, Anterior peritoneal sac. *C*, Stomach. *D*, Aortic opening. *E*, Post intercrural muscle. *F*, Transverse membrane of central tendon of diaphragm. *G*, Muscle band arising from the left crus and passing to the right hiatal limb.

approaches the sagittal diameter in size. The essential anatomic difference between the normal hiatus and that associated with a hernia is the increase in the transverse diameter. Associated with the widened hiatus there is an increased separation of the posterior hiatal limbs so that, in place of the normally acute angle formed by the divergence of the right and left hiatal limbs, an obtuse angle may be present (Figs. 6 and 7). The quality of the crural muscle is often surprisingly good even when a large hernia is present.

Other anatomic changes such as the attenuation of the esophagophrenic ligament, elongation of the posterior gastric vessels, and the development of an anterior hernial sac have been frequently described and are generally accepted (Table II).

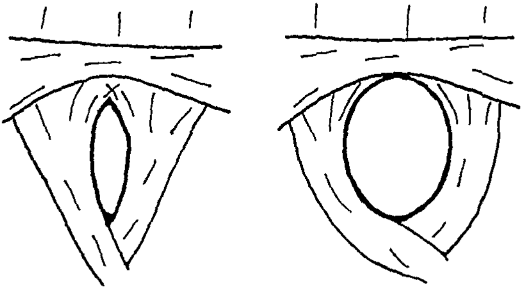

Fig. 7.—Diagram to show the differences bet and one which is
the site of a hernia. The anterior rim of muscle is ded and the hiatal
limbs are divaricated posteriorly. The surface when the hiatus
widens and extrinsic support to the cardia is then

TABLE II. COMPARISON BETWEEN THE NORMAL AND ABNORMAL HIATAL ANATOMY

	NORMAL ANATOMY	HIATUS HERNIA
Size	Admits 1-2 fingers	Admits 3 4 fingers
Shape	Saggital ellipse	Circular opening
Anterior decussating fibers	Present	Absent or atrophic
Posterior muscle bands	"Semi-closed scissor" position	"Open scissor" position
Hiatal muscle limbs	Generally well developed	Often well developed
Esophagophrenic ligament	Easily definable	Poorly definable
Posterior mesoesophagus (left gastric artery and vein)	Taut	Lax
Anterior peritoneal pouch	Absent or admits finger tip	Admits 2 or 3 fingers easily

DISCUSSION

A previous paper reported a series of experiments designed to measure the forces which the diaphragm has to withstand during life.[15] The pleuroperitoneal pressure gradient constantly tends to extrude the abdominal contents into the chest and, during deep inspiration and postural change, the pressure may be very considerable. The effect of these physiologic actions is enhanced by pregnancy, obesity, and any other cause of ''packing'' of the abdominal contents. The intra-abdominal pressure affects the whole diaphragm, but only the esophageal hiatus is vulnerable because it faces directly into the peritoneal cavity. Also, the liver proffers it no protection and its anterior edge is unsupported on the thoracic side. The hiatus transmits the esophagus which does not occupy the opening tightly and which guides the mobile stomach directly into it. The integrity of the hiatus, therefore, depends essentially upon its intrinsic structure where a fine balance between mobility and stability is attained. Competence is primarily dependent upon the size and shape of the hiatus and these are maintained at optimal dimensions by the tethering action of the anterior decussating muscle fibers and the crossover of the crura. So long as the hiatus remains small the hiatal limbs with their membranous reinforcements act as buffers against the positive peritoneal pressure and so protect the esophagophrenic ligament from continuous strain. Most of the intrinsic strength of the hiatus is placed in front of the esophagus. Here the anterior decussating fibers are supported by the transverse membrane of the central tendon and the phrenoesophageal ligament is well developed and cordlike. There is less provision for strength behind where the hiatus is less vulnerable. At the posterior hiatal boundary, the crura are still ascending steeply and are firmly supported by the vertebral column; also, this area is separated from the peritoneum by a cushion of fat and by the extraperitoneal portion of the stomach. Only the anterior ends of the hiatal muscles are therefore exposed to the full force of the pressure exerted from below while distention of the esophagus caused by gastroesophageal reflux tends to widen the hiatus transversely and throw additional strain upon the anterior decussating fibers. If these should disrupt, the hiatus will assume a circular contour, its surface area will greatly increase, and the support for the cardia and the peritoneal reflection will be lost. Once deprived of hiatal support the peritoneum will tend to bulge upward into the mediastinum in front of the esophagus and the phrenoesophageal ligament will now be exposed to the unbuffered force of the intraperitoneal pressure. Should this ligament stretch, as it inevitably must, the cardia will displace upward into the mediastinum. Occasionally the phrenoesophageal ligaments and the left gastric vessels retard the cardia while the gastric fundus rolls into the peritoneal sac. In this way a para-esophageal hernia forms, but this is simply a variant of the sliding hernia. In my experience, it is excessively rare for a ''rolling'' hernia to be unaccompanied by some degree of upward slide of the cardia.

This concept of the pathogenesis implies that adult hiatus hernia is an acquired malady. This view is supported by the age of onset of the condition. Allison[2] has stated that symptoms characteristically develop in the fifties. We have records of 25 men and 40 women who could clearly recall when first they experienced troublesome dyspepsia and the average age of onset of symptoms in the men was 44 and in the women 42. Rigler and Eneboe,[16] Evans and Bouslog,[8] Dutton and Bland[7] and many others feel that, in many cases, pregnancy is an etiologic factor. Of our 54 women patients only 2 had never been pregnant and 46 of the remainder (92 per cent) could recall severe symtoms of flatulent dyspepsia during their pregnancies. It is believed that flatulent dyspepsia is invariably due to gastroesophageal regurgitation and that this reflects weakness or strain of the gastroesophageal "sphincter" mechanism.[14] Conditions during pregnancy would seem to be ideally conducive to the development of hiatus herniation. As the gravid uterus enlarges, the abdominal contents are compressed and a pronounced rise in the basal intraperitoneal pressure results. In addition, a profound physiologic effect is exerted upon the collagenous components of the body by a circulating hormone derived from the corpus luteum and placenta. Softening of the collagen in membranes, ligaments, and muscles results and they then tend to stretch in the face of the high abdominal pressures of pregnancy and labor. Rigler and Eneboe[16] subjected 195 women, chosen at random, to barium meal examinations during the third trimester of pregnancy and were able to demonstrate hiatus hernia in 5.1 per cent of primiparas and 18.1 per cent of multiparas. They re-examined 10 patients after parturition and in 4, hernias were still present. These results are highly significant particularly in view of the rigidity of their radiologic criteria for diagnosis and the inadequacy of their technique. During their examinations they made no attempt to raise the abdominal pressure except through coughing and straining. Such actions do not increase the pleuroperitoneal pressure gradient markedly[14, 15] and after parturition, when the abdominal wall is lax, it is necessary that an artificial method of increasing the intraperitoneal pressure should be used before the existence of a hernia is excluded.[12] It is probable that more of Rigler and Eneboe's patients would have shown hernias postnatally had a compression appliance been used. The author has seen 3 multiparous women in the late stages of pregnancy who experienced intractible vomiting caused by hiatus hernias. In each case the persistence of the hernia was confirmed with the aid of sustained abdominal compression from 3 to 6 months after parturition.

Many hiatus hernias must go unrecognized during pregnancy because symptoms of gastroesophageal regurgitation are disregarded, even by the medical attendant. It is true that the symptoms regress after parturition but they tend to recur with subsequent pregnancies or with gain in weight. With 4 of my cases, recurrence of dyspepsia has coincided with the development of pathologic abdominal tumors.

One interprets the course of events as follows: During pregnancy the cardia may herniate through the esophageal hiatus as a result of the softening of the restraining membranes and the raised abdominal pressure. Following parturition, the intraperitoneal pressure is suddenly diminished and the softened body collagen starts to involute. It is generally agreed that stability is restored within 6 months but should membranous and elastic fibers be overstretched or ruptured, they never regain their previous strength. If this has happened to the muscle and membrane of the hiatus, full restitution of the stability is unlikely. However, because of the now capacious abdomen with lax abdominal musculature the regurgitating force has been dissipated and only when the individual subsequently gains weight and increases her abdominal pressure, do dyspeptic symptoms recur.

Another important etiological factor is obesity. This, by causing "packing" of the abdominal viscera particularly if good abdominal muscle tone is retained, may so raise the basal intraperitoneal pressure as to overcome the intrinsic stability of the esophageal hiatus. We have kept records of the recollected age, height, weight, and basic build of 25 male and 40 female patients at the time when first they experienced symptoms of reflux dyspepsia. With this data it is possible to estimate the ideal weight for a given age and body build. The standard tables recommended by the Metropolitan Insurance Company[19] have been consulted for this purpose. The results of analysis indicate that a high proportion of patients with hiatus hernia first develop dyspepsia when they are overweight. Only one woman (2 per cent) was below ideal weight while 73 per cent were significantly heavier than desirable and 34 per cent were obese. There were fewer obese men in the group but the percentage who were more than 10 per cent above ideal weight was approximately the same as the women (65 per cent and 73 per cent). Among the men who were overweight, there were many who were of powerful build rather than fat. This is too subtle a distinction to analyze statistically, but the strong impression remains that men who retain good abdominal muscle tone are subject to hiatus hernia when they put on weight. It is not suggested that the first symptoms of reflux dyspepsia indicate the presence of a hernia. One agrees with Donnelly[6] that symptoms of flatulent dyspepsia may precede the development of herniation by many years, but it is considered that the causes which produce gastroesophageal regurgitation will also eventually disrupt the esophageal hiatus.

Although pregnancy and obesity are the two common causes of hiatus herniation, they are not necessarily the only ones. Any cause of weakening of the anterior muscle and membrane of the hiatal mechanism may result in herniation. Congenital deficiencies, trauma, or the degeneration of senility could all be responsible. Long-continued increase of the abdominal pressure caused by pregnancy, obesity, abdominal tumors, pyloric spasm, and constricting garments, by exerting an intractable strain upon the exposed anterior edge of the hiatus, may also eventually disrupt the hiatus. In many cases, both basic factors, namely an increased herniating force and a weakened defensive mechanism, will be simultaneously responsible.

Treatment, to be rational, must be directed either toward repair of the anterior defect and the accessory ligaments or to reduction of the herniating force. The first can only be accomplished surgically and the latter medically unless a pathologic tumor is present. Weight reduction can never cure a hernia, yet, by lessening gastroesophageal regurgitation, it may so reduce the symptoms that nothing further need be done. The effectiveness of a pronounced diminution of the regurgitating force is unquestionable, as is instanced by the disappearance of symptoms of reflux dyspepsia after parturition. However, it is believed that once the complications of reflux esophagitis or fundal ulceration are present one's decision as to treatment should be biased in favor of surgical repair It must be remembered that the intra abdominal pressure is the herniating force, and in order to protect the stability of his repair a surgeon is wise to insist upon pre and postoperative weight reduction

SUMMARY

1 Thirty diaphragms have been dissected The anatomy of the esophageal hiatus of the diaphragm is described

2 The reasons for the susceptibility of the hiatus to herniation are analyzed It is concluded that stability is dependent upon the narrow size and oblique shape of the hiatus The crossover of the crural limbs, the decussating muscle fibers, and the transverse membrane of the central tendon of the diaphragm are the major protective structures in that they maintain the size and shape of the hiatus at optimal dimensions The phrenoesophageal ligament tethers the cardia at diaphragm level but once the hiatus dilates it becomes subject to the full strain of the peritoneal pressure and inevitably it will stretch

3 The intraperitoneal pressure is the force which tends to produce gastroesophageal regurgitation The same pressure is also the force which extrudes the stomach into the mediastinum The effective herniating force is the pleuroperitoneal pressure gradient and this varies physiologically and pathologically The causes of such variation have been discussed elsewhere[15]

4 There is a life long antagonism between the herniating force and the anatomic resisting mechanism of the hiatus Herniation can occur when the herniating force is increased over a long period of time or when the resisting mechanism is weakened, often both causes are present together Pregnancy and obesity are the commonest conditions which produce herniation in the adult

I am grateful to Mr L Fatti, Head of the Department of Thoracic Surgery of the Johannesburg Hospital, for allowing me to investigate and treat many of his patients The illustrations were reproduced by the Photographic Unit of the Department of Medicine, University of the Witwatersrand

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RECONSTRUCTION OF THE THORACIC AORTA WITH THE AID OF A VASCULAR COUPLING DEVICE (VESSEL COUPLE)

Report of a Case

Timothy Takaro, M.D.,[*] *and Thomas P. Crymes, M.D.,*[**] *Oteen, N. C.*

To circumvent the dual problems of spinal cord ischemia and cardiac strain attendant upon occlusion of the upper descending thoracic aorta during reconstructive surgery, intraluminal[1,2,3] and extraluminal[4-7] shunts, hypothermia,[8,9] and extracorporeal circulation[10,11,12] have all been used with success. Additional techniques have been suggested by the work of Fryfogle and his associates,[13] and by that of Villegas,[14] Kelly and Alden,[15] and Tibbs and Leslie.[16] These surgeons have designed devices which make possible rapid approximation of the opened ends of vessels or of vessels and grafts, with minimal interruption of blood flow. A leisurely suture-anastomosis in a more or less conventional manner is then possible while blood is flowing through the vessels being anastomosed. Subsequently, the devices are removed. A number of nonsuture techniques have also been suggested[17,18,19] but, in two of these, the devices are left permanently in the vessel. This is usually not a desirable feature.

An additional technique is presented in this report, based on a new coupling device After experience with it had been gained with 40 animals in the experimental laboratory, it was applied clinically in a patient with a syphilitic aneurysm of the upper third of the descending thoracic aorta.

The instrument, designed by one of us (T. T.), is essentially a vascular clamp made up of two cylindrical jaws of unequal length, bivalved to permit removal, and carrying fine teeth on one or two apposing ridges.[†] Two bolts which fit into perforated, slotted wings on the cylinders, make it possible to adjust the distance between the jaws of the clamp, and also to hold together the halves of each cylinder (Fig. 1). The technique of application of the clamps is illustrated in Fig. 2. The important feature to be noted is that the edges of both the vessel and the graft to be anastomosed present themselves between the jaws of the clamp, and are thus available for suturing under direct vision.

From the Cardio-Pulmonary Research Section, Veterans Administration Hospital, Oteen, N. C.

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[*] Chief, Clinical Research and Resident Education Section, Surgical Division.

[**] Chief, Cardiovascular Surgery.

[†] Manufactured by A. W. Chattaway, Asheville Tool and Gauge Company, Asheville, N. C.

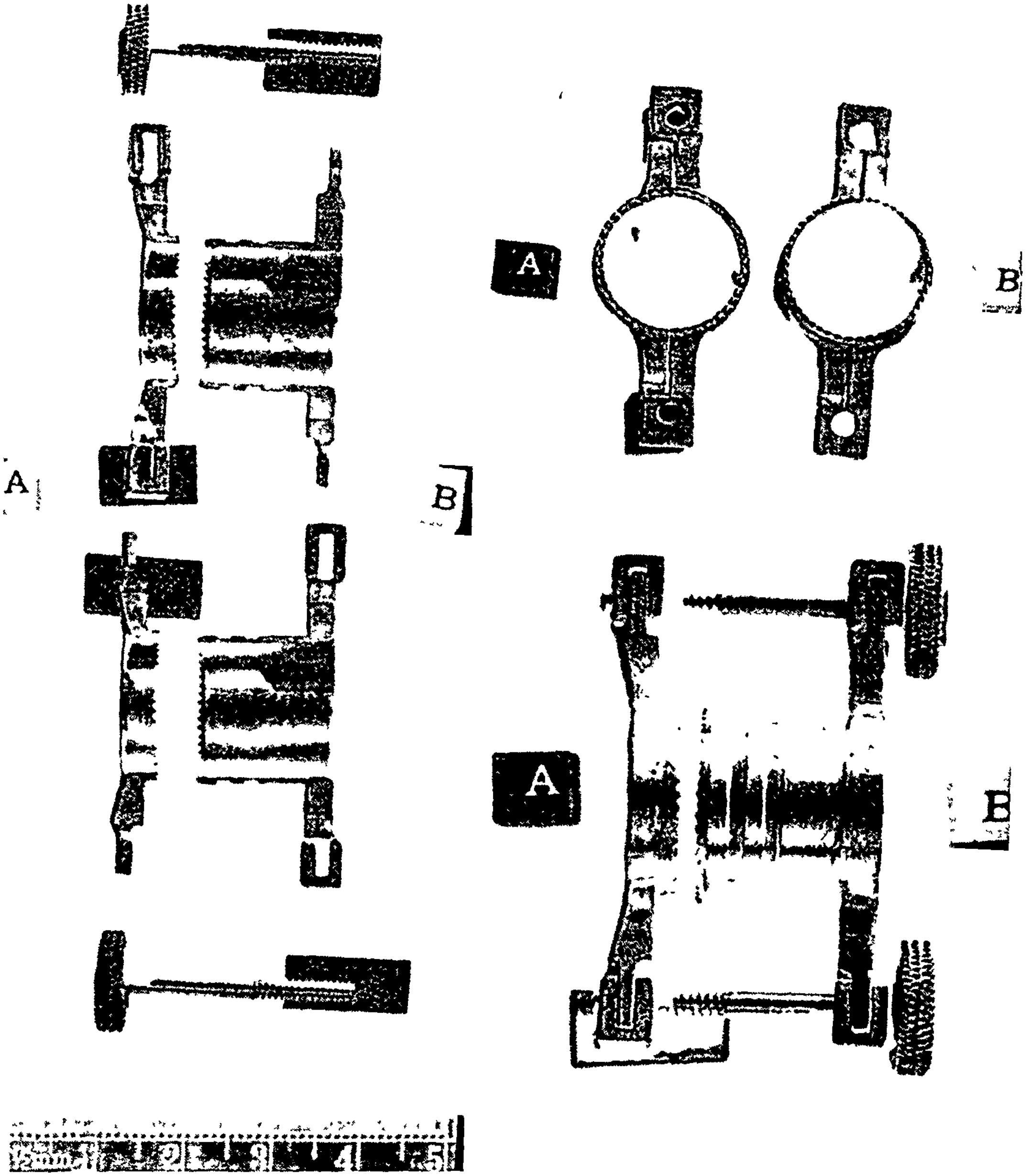

Fig. 1.—The vessel couple disassembled, and assembled.

A, Extraluminal jaw bearing fine teeth on two ridges with V-shaped groove between them.

B, Intraluminal jaw, or graft-bearing portion of couple, bearing fine teeth on a single ridge, which fits into the groove of the opposite jaw. In addition, on the shank of the cylinder there are two square-cut grooves, one to hold a temporary graft-everting ligature, and the other for a temporary wire snare to hold the vessel cuff on the couple until the bolts can be placed. The two bolts adjust distance between jaws, and also serve to hold the halves of each jaw together.

Fig. 2.—Technique of anastomosis using vessel couples.

A, Host vessel prepared to receive graft-bearing portion of vessel couple. The extraluminal jaw is in place around the vessels and held together with temporary ligatures. Stay sutures steady the edge of the vessel. Both of these steps are usually done before blood flow is interrupted. After temporary occlusion of the blood vessel, it is opened over half its circumference. It is not divided completely.

B, Intraluminal or graft-bearing jaw with nylon graft held everted on the couple with a temporary ligature gripping the first groove. This holds the halves of the couple together as well.

C, Host vessel pulled over intraluminal graft-bearing jaw of the couple and held in place with temporary wire snare gripping second groove, until bolts can be put into place and secured.

D, Vessel couple holds vessel and graft securely by multiple fine teeth on interdigitating ridges. The wire snare, the stay sutures in the edge of the vessel, and the ligature holding the graft everted on the intraluminal jaw have all been removed. Blood flow has been re-established, and suturing of the edge of the vessel and the edge of the graft under direct vision has been started.

E, The completed anastomosis—an everting suture line, following removal of the couples. A similar process is ordinarily carried out on the other end of the graft.

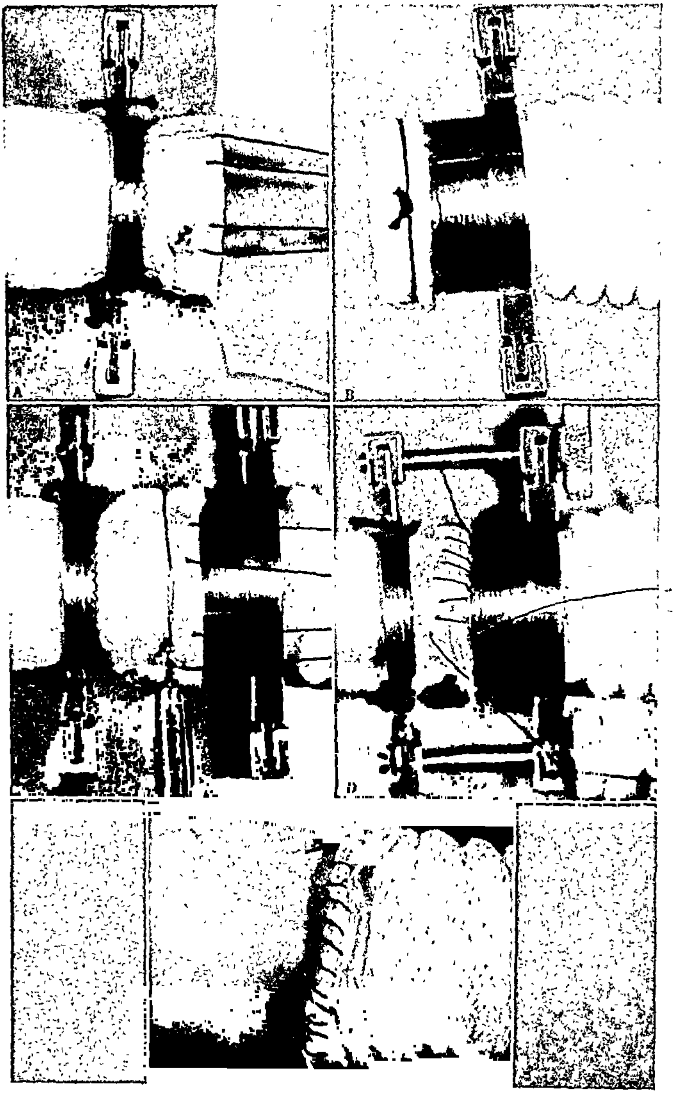

Fig. 2, *A-E.—For legend see opposite page.*

A vessel couple with an internal diameter roughly two thirds to three fourths that of the external diameter of the blood-filled aorta has been found by experience to be about the correct size.

CASE REPORT

R. E., a 64-year-old white man, was admitted to the Veterans Administration Hospital, Oteen, N. C., with a 2-year history of left chest pain. A mediastinal mass, which had not been seen on a roentgenogram of the chest 5 months previously, was noted by the referring attending physicians at the VA Hospital, Beckley, West Virginia. Subsequent investigations revealed that the patient had received treatment for syphilis some 30 years previously; that he had been subject to seizures of the grand mal type during the past 3 years; and that his wife had noted gradual mental deterioration over the past several years. The patient had suffered a cerebral concussion in an auto accident in April, 1955.

The physical examination was not remarkable. A pulsating posterior mediastinal mass was seen at fluoroscopy, and cardioangiography, using a technique described by McCaughan and Pate,[20] showed this to be an aneurysm involving the upper descending thoracic aorta just distal to the origin of the left subclavian artery. Laboratory studies were unremarkable except that the VDRL serological reaction was positive in a dilution of 1 to 64 and the Kolmer was positive 4 plus in both blood and spinal fluid.

Resection of the thoracic aneurysm was carried out on March 7, 1958, through a left posterolateral thoracotomy incision. An 8 by 15 cm. fusosacciform aneurysm originating in a widened portion of the aorta, 1.5 cm. beyond the origin of the left subclavian artery, was dissected almost completely free of the lung, vertebral column, and esophagus. The largest available vessel couple (2 cm. internal diameter) was prepared with a 15 cm. length of specially manufactured Edwards-Tapp crimped nylon fabric tubing, 2.5 cm. in diameter,* for insertion into the aorta distal to the aneurysm. At the site of the distal anastomosis the aorta measured 3.2 cm. in diameter. A larger couple was not available for use proximally where the aorta measured 4 cm. in diameter and, in any event, the short distance between the aneurysm and the origin of the left subclavian artery would not have permitted use of a couple at this point. The aorta was occluded above and below the aneurysm and divided above. An anastomosis between the nylon graft and the proximal aorta was carried out using a simple over-and-over running suture of 4-0 silk. This anastomosis together with some necessary brief dissection after division of the aorta occupied 25 minutes.

The aneurysm was then laid open down to normal distal aorta, around which the extraluminal jaw of the vessel couple had previously been placed. The graft-bearing intraluminal jaw was then inserted into the incompletely divided end of the distal aorta, and held in place temporarily with a wire snare. The bolts approximating the jaws of the clamp were applied and tightened and the occlusive clamps on the aorta above and below the aneurysm were removed, re-establishing blood flow, which was now directed through the graft. These maneuvers occupied 7 minutes. There was considerable hemorrhage through the interstices of the graft despite ''pre-clotting'' in a basin of fresh blood before use, and marked hypotension for a brief period of time resulted. There was no bleeding between the jaws of the couple.

The aneurysm was next freed completely from its remaining attachments to the distal aorta and the esophagus, and removed. After dividing and removing the temporary ligature which held the graft everted on the vessel couple, the edges of both the aorta and the graft were available for suturing. An anastomosis was carried out between them, using the same simple running over-and-over suture of 4-0 silk. An everting suture-line resulted. The vessel couple was then removed. Bleeding from the anastomosis was minimal. The only feature which marred the final result was rather marked bowing of the nylon graft, due to stretching of the prosthesis associated with the large volume of blood flow at high pressure. This made it impossible to cover the graft with mediastinal pleura. The wound was closed, and both pleural cavities drained with negative pressure.

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*Generously donated by the U. S. Catheter & Instrument Co., Glens Falls, N. Y.

The patient reacted promptly and *moved all his extremities vigorously. He was oliguric* for 2 days, but thereafter excreted over a liter of urine daily. Blood urea nitrogen rose to 56 mg. per cent on the fifth day, and declined thereafter. Since there was no evidence of damage to the spinal cord, his transient oliguria and azotemia were attributed to the period of hypotension during surgery. The left recurrent laryngeal nerve had apparently been injured by dissection or traction during the operation, and there was hoarseness and aspiration of food and fluids. A tracheostomy was done on the third postoperative day and oral intake stopped. Nevertheless, the patient developed a fulminating bilateral bronchopneumonia due to a hemolytic *Staphylococcus aureus*, resistant to all antibiotics except Furadantin and Magnamycin, and died on the ninth postoperative day.

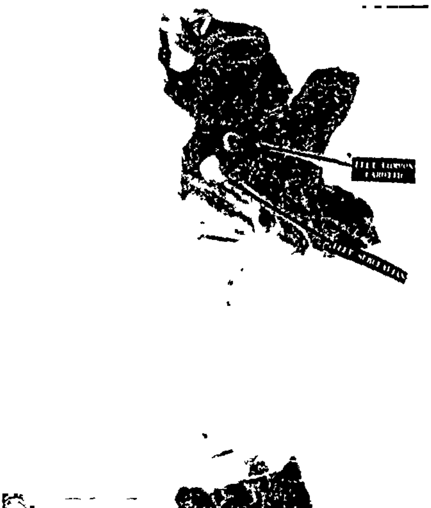

Fig. 3.—Autopsy specimen showing nylon graft in descending thoracic aorta, which had functioned perfectly for 9 days until death due to staphylococcal bronchopneumonia. The proximal anastomosis, at the top of the photograph, was made in the conventional manner; the lower anastomosis was made with the aid of a vessel couple while blood was flowing through the graft.

An autopsy was done. This showed bilateral suppurative bronchopneumonia, and a small localized empyema at the right anterior thoracotomy site. There was evidence of a *mild to moderate nephrosis. The graft was intact and had apparently functioned well. The* proximal anastomosis was technically satisfactory and the distal anastomosis was excellent (Fig. 3).

DISCUSSION

Although shunts, hypothermia, and extracorporeal circulation have been used with success in treating aneurysms in this area, serious complic accompany the use of all of these methods. Thus, the continued search for other techniques which might be used independently or in conjunction with the three mentioned above.

The technique presented allows the surgeon ample time to anastomose vessels and grafts, the ends of which are under direct vision for suturing while blood flows through the vessels being united. In using the Fryfogle vessel couples, we have been uneasy with the blind suturing method required, and unhappy with our results in the experimental laboratory. These difficulties are compounded with diseased, thickened vessels, and heavy graft material. We have had no experience with the other couples which have been described in the literature.

If a long enough cuff of vessel proximally is not available to allow use of the vessel couple for the definitive graft, by-pass shunts can be placed rapidly with this device, using the left subclavian artery proximally, and the descending aorta distally. After the proximal anastomosis of the definitive graft has been made in the conventional manner, the shunt can be uncoupled distally, and the distal end of the graft coupled to the aorta in its place. Similarly, use of vessel couples in conjunction with hypothermia or extracorporeal circulation might shorten the time of application of these techniques and thus perhaps increase the margin of safety for the patient.

We are currently engaged in the laboratory in replacing the arch of the aorta in dogs and in suturing Hufnagel valves into the thoracic aorta with the aid of vessel couples. These experiments and the details of the laboratory work leading to the development of the technique described in this paper will be reported elsewhere. Modifications of the design of this coupling device, and other applications of this and other devices with similar aims will undoubtedly occur to surgeons interested in this field.

SUMMARY

A technique for reconstructing the thoracic aorta using removable vessel couples of special design, with minimal interruption of blood flow, is described. A conventional suture-anastomosis can be made while blood is flowing through the vessels to be joined, since the ends of the vessels are available between the jaws of the clamp for suturing under direct vision. This technique was successfully applied in reconstruction of the upper descending thoracic aorta in a patient with a syphilitic aneurysm, using a crimped nylon fabric seamless-tube prosthesis. However, the patient died on the ninth postoperative day of a fulminating staphylococcal bronchopneumonia.

We wish to acknowledge the assistance of Mr. Robert P. Ramer of Sangli, India, of Mr. Harry Smith, Miraj, India, and of the Bombay Surgical Company, Bombay, India, in the development of some of the earlier models of our vessel couple.

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PRESSURE MEMBRANE OXYGENATOR

Ibrahim K. Dagher, M.D., Beirut, Lebanon

Many varieties of artificial pump-oxygenators for total cardiopulmonary bypass have been described. All are variants of one of the main three types: the film,[5, 7, 8] the bubble,[3, 4] and the membrane oxygenator.[1, 3] Each one of these methods of oxygenating blood has its limitations. Common to the first two varieties is the existence of the gas blood interface which has been demonstrated to denature the blood proteins.[2] The membrane oxygenator protects the extracorporeal blood from the gaseous oxygen and prevents air embolization. Its efficiency is limited by the ability of the membrane to allow the exchange of gases between the blood and its ambient medium. This limitation has been partially compensated for by the increase of the membrane surface exposed to the blood.[1] Consequently the size of the apparatus and its priming volume increased.[10] The purpose of this paper is to describe a pressure membrane oxygenator capable of diffusing four times more oxygen than has previously been reported.[1] Thus, the size of the apparatus and its priming volume can be proportionately decreased.

PRINCIPLES

On the basis of the kinetic molecular theory of gases it can be shown that the number of moles (M) of a gas at a given pressure diffusing through a surface (S) of a membrane of a known thickness (Z) during a period of time (T) can be represented by the formula[11]:

$$M = \frac{K \times S \times (P1 - P2)\ T}{\sqrt{\text{Mol. Wt.}} \times Z}$$

Where K = Constant of porosity of the membrane.
P1 = Pressure of gas on one side of the membrane.
P2 = Pressure of gas on the other side of the membrane.
Mol. Wt. = Molecular weight of the gas.

If, in the above formula, the constants are eliminated the volume (V) of a gas diffusing through the membrane per unit time per unit surface area will

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From the Surgical Research Laboratory, Department of Surgery, American University of Beirut, School of Medicine, Beirut, Lebanon.

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be proportional to the pressure gradient between the two surfaces of the membrane:

$$V \sim P1 - P2.$$

The rate of diffusion of carbon dioxide dissolved in the blood will follow Graham's law and will be proportional to the difference in partial pressure of carbon dioxide on the two sides of the membrane and inversely proportional to the square root of its molecular weight.[6]

It is these principles which have been applied in the construction of the proposed "pressure membrane oxygenator."

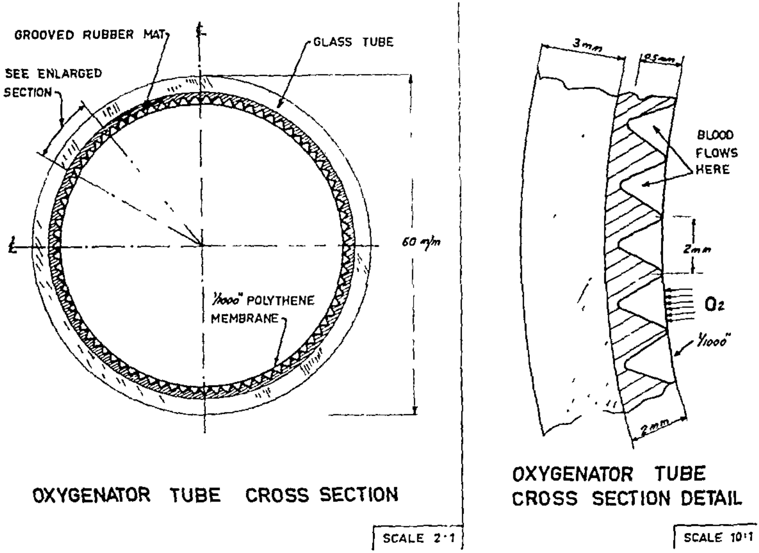

Fig. 1.—Engineering drawing of a cross section at the middle of the oxygenating unit.

MATERIAL AND METHODS

A cylindrical polyethylene (Polythene) membrane 0.00254 cm. (0.001 inch) in thickness was tested against pressure and its rupturing point determined. Its ability to diffuse oxygen and carbon dioxide under a given pressure was measured and compared with the results obtained by other investigators.[1] A measured volume of fresh canine venous blood was circulated around the membrane for a definite period of time. The oxygen and carbon dioxide content of the venous and arterialized blood was determined by the method of Van Slyke and Neill,[13] and the pH was determined with a glass electrode (Beckman pH meter). The pressure and the flow of oxygen through the polyethylene cylinder were regulated and measured by a pressure meter and a flow meter.

The blood pressure in the plastic (Mayon) tubing between the venous head of the Sigmamotor pump and the oxygenating unit was monitored with a mercury manometer. All parts of the setup coming in touch with the blood, except the polyethylene membrane, were siliconized.

PROCEDURES

Pressure Membrane Oxygenator.—A cylindrical polyethylene membrane, 0.00254 cm. in thickness, 4.9 cm. in diameter, and 100 cm. in length, presenting a diffusing surface area of 0.154 M.^{2}, was fastened over a rubber stopper on one end and was introduced into a 100 cm.-long glass tube into which a rubber mat with longitudinal grooves had been placed (a grooved plastic tube would have been easier to handle). The other end of the membrane was fastened in a similar fashion around another rubber stopper so that all the membrane was supported by the rubber mat. Each of the rubber stoppers had a central hole into which was introduced a 15 cm.-long stainless steel connector. A sleeve of siliconized rubber was fixed to both ends of the outer glass tube and was closed with a rubber stopper with two holes. The central hole admitted the stainless steel connector that had already been introduced into the single hole of the rubber stopper around which the polyethylene membrane was fixed. The other hole admitted a stainless steel connector that directed the blood into and away from the oxygenating unit. A short distance, 3 to 5 cm., was left between the

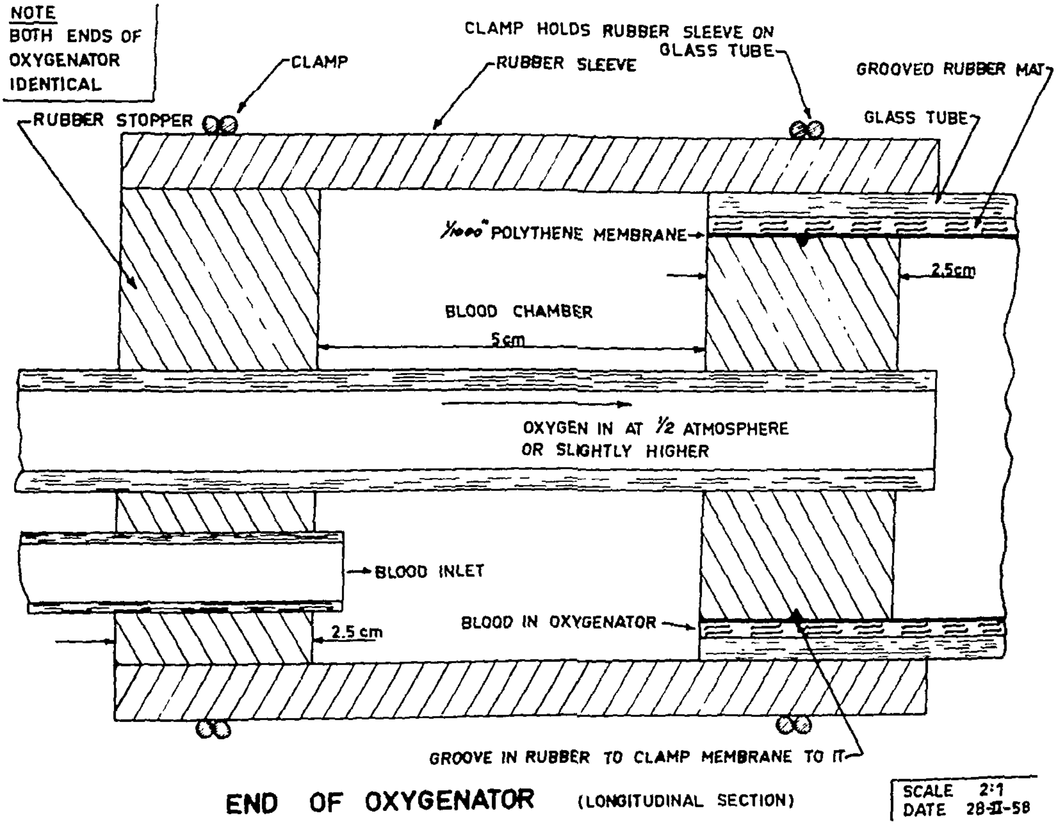
NOTE
BOTH ENDS OF OXYGENATOR IDENTICAL
CLAMP
RUBBER SLEEVE
CLAMP HOLDS RUBBER SLEEVE ON GLASS TUBE
GROOVED RUBBER MAT
RUBBER STOPPER
GLASS TUBE
1/1000" POLYTHENE MEMBRANE
2.5cm
BLOOD CHAMBER
5cm
OXYGEN IN AT ½ ATMOSPHERE OR SLIGHTLY HIGHER
BLOOD INLET
2.5 cm
BLOOD IN OXYGENATOR
GROOVE IN RUBBER TO CLAMP MEMBRANE TO IT
END OF OXYGENATOR (LONGITUDINAL SECTION)
SCALE 2:1
DATE 28-II-58

Fig. 2.—Engineering drawing of a longitudinal section at the end of the oxygenating unit.

two rubber stoppers on each end to allow the blood to find its way into and away from the grooves around the membrane (Figs. 1 and 2). The central stainless steel connector on one end was attached to an ordinary oxygen tank with a pressure-reducing flow meter. The central connector on the other end was wired to a rubber tubing with two side-branchings. A Hoffman infusion clamp was applied on one branch and the other branch was attached to a pressure meter. The oxygen flow meter was opened until it marked 8 L. per minute and the Hoffman clamp was tightened until the pressure meter read 500 Gm./sq. cm. At this pressure, the oxygen flow meter usually recorded 3 to 4 L. per minute. Isotonic saline solution was then pumped into the system until all the air was driven out. Four hundred and fifty milliliters of fresh canine venous blood was used to displace the saline solution. The tubes were connected with a stainless steel connector creating a closed system with a bubble trap on the arterial end of the oxygenating unit (Fig. 3). In each experiment the blood was circulating around the membrane for 4 consecutive minutes. Blood samples for analysis were taken at the start and at the end of each perfusion experiment.

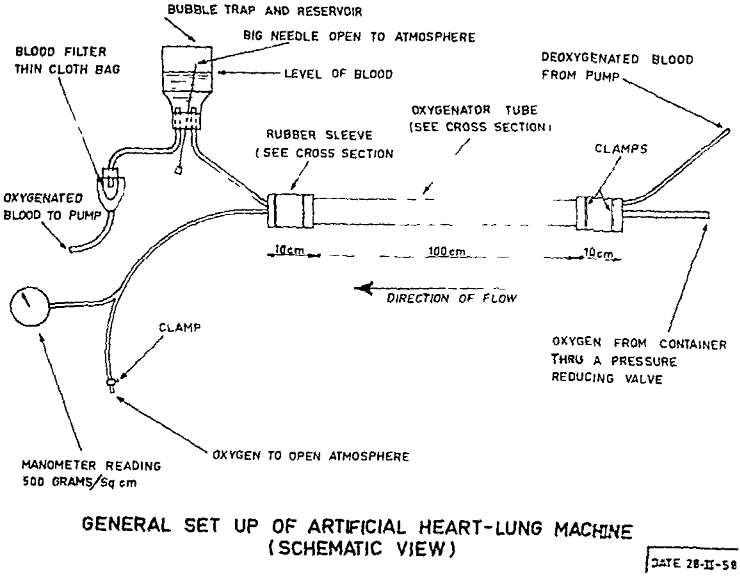
BUBBLE TRAP AND RESERVOIR
BIG NEEDLE OPEN TO ATMOSPHERE
BLOOD FILTER THIN CLOTH BAG
LEVEL OF BLOOD
DEOXYGENATED BLOOD FROM PUMP
OXYGENATOR TUBE (SEE CROSS SECTION)
RUBBER SLEEVE (SEE CROSS SECTION
CLAMPS
OXYGENATED BLOOD TO PUMP
10cm
100 cm
10cm
DIRECTION OF FLOW
CLAMP
OXYGEN FROM CONTAINER THRU A PRESSURE REDUCING VALVE
OXYGEN TO OPEN ATMOSPHERE
MANOMETER READING 500 GRAMS/Sq cm
GENERAL SET UP OF ARTIFICIAL HEART-LUNG MACHINE
(SCHEMATIC VIEW)
DATE 28-II-58

Fig. 3.—Engineering drawing of the general set of one oxygenating unit when assembled.

RESULTS

The unsupported polyethylene cylinder stood a pressure of 200 Gm. [illegible] cm. Above this pressure, it dilated and proceeded to rupture. When supported by the grooved cylinder, the membrane stood a pr [illegible]

TABLE I. TABLE OF RESULTS*

EXPERIMENT	VENOUS BLOOD OXYGEN ML. % AND % SATURATION	ARTERIAL BLOOD OXYGEN ML. % AND SATURATION	VENOUS BLOOD (CO_2 mM/L.)	ARTERIAL BLOOD (CO_2 mM/L.)	VENOUS BLOOD (pH)	ARTERIAL BLOOD (pH)	DIFFUSION (ML./M.^{2}/MIN.)	PRESSURE (GM./SQ. CM.)
I	12.74 72.8%	17.42 99.54%	34.8	17.0	7.24	7.3	35.10	500
II	18.24 75%	22.32 93%	34.8	15.1	7.20	7.28	30.0	500
III	19.76 89.94%	21.97 100%	15.26	14.64	7.30	7.40	Bubble formation	500
IV	20.73 94.3%	21.97 100%	14.45	13.8	7.28	7.35	Bubble formation	500
V	14.4 60%	18 75%	31.0	14.64	7.26	7.34	53.3	1,000
VI	14.22 59%	17.82 74%	32.0	13.8	7.22	7.34	53.3	1,000

*Four hundred and fifty milliliters of blood was circulated for 4 minutes around a surface area of 0.154 M.^{2} of a polyethylene membrane, 0.00254 cm. in thickness.

cm. At this pressure, however, the membrane wedged itself into the furrows of the mat. The resistance to the circulating blood was thus increased and the pressure in the plastic tubing between the venous head of the pump and the oxygenating unit reached 360 mm. of mercury. At this same pressure, the diffusion of oxygen through the membrane was 53.3 ml./M.^{2}/min. At a pressure of 500 Gm./sq. cm. the pressure of the blood between the venous head of the pump and the oxygenating unit was 180 mm. of mercury. At this pressure the oxygen diffusion averaged 32.5 ml./M.^{2}/min. The carbon dioxide content of the venous blood averaged 27.05 mM/L. and that of the arterialized blood 14.49 mM/L. The pH of the arterialized blood went up to 7.33 ± 0.01 as compared with 7.25 ± 0.01 for the venous blood.

In another set of experiments in which blood with a relatively high oxygen content (19.76 V per cent, 89.94 per cent saturated, and 20.73 V per cent, 94.30 per cent saturated) was used, it was found that the blood became fully saturated (21.97 V per cent) and fine bubbles appeared in the tubing system. These results are presented in the accompanying table (Table I).

DISCUSSION

The crests of the grooved mat over which the polyethylene membrane lies not only support the membrane, preventing it from rupturing at a pressure of 500 Gm./sq. cm., but also prevent it from wedging into the grooves. Thus, the blood will pass through the grooves around the membrane and pick up the diffused oxygen without having the pressure inside the membrane transmitted to it.

The diffusion of oxygen across the membrane is directly proportional to the pressure gradient between the two surfaces of the membrane (P1 – P2). Whereas at atmospheric pressure 7.6 ml. of oxygen was reported to diffuse across one square meter per minute, at a pressure of 500 Gm./sq. cm. above atmospheric pressure an equal surface of a membrane of the same thickness and chemical composition diffused 32.5 ml. of oxygen per minute. This represents an increase in diffusion efficiency of 427 per cent. At a pressure of 1,000 Gm., the diffusion efficiency became 705 per cent. At such a high pressure a thicker membrane is less likely to wedge into the grooves and the blood will circulate without any increase in the resistance to its flow.

In the experiments in which the circulating blood could not dissolve and combine with all the diffused oxygen, the formation of homogeneously distributed microbubbles was noticed. The bubbles represent the increment of oxygen diffused over the oxygen dissolved in, and combined with, the blood. From these experiments it is concluded that the volume of blood circulating around the membrane should have the ability to dissolve and combine with all the oxygen diffused in order to prevent the formation of bubbles. The formation of these bubbles can be prevented either by increasing the circulating blood volume (and this is limited by the volume of the venous return), or by decreasing the pressure inside the membrane. As an added safety measure a bubble trap has been included in the circuit to allow the escape of such bubbles and to act as a reservoir for blood.

The carbon dioxide elimination was very effective. Although the pressure inside the membrane was 500 Gm./sq. cm., the partial pressure of carbon dioxide was zero and its elimination from an average of 33 mM/L. in the venous blood to 14.6 mM/L. in the arterial blood is the result of the high pressure gradient between the two surfaces of the membrane. In spite of the high rate of carbon dioxide diffusion the pH of the blood did not change appreciably. It went up from 7.24 ± 0.01 to 7.33 ± 0.01. This low carbon dioxide content plus a normal pH is similar to a state of compensated respiratory alkalosis which can be prevented by mixing carbon dioxide with the oxygen in order to decrease the pressure gradient of carbon dioxide.

In order to have a diffusing surface large enough to provide a sufficient amount of oxygen to saturate all the venous return, several oxygenating units can be assembled in parallel. This arrangement increases the "mechanical efficiency" of the system by increasing its surface of diffusion and decreasing its total resistance to the blood flow according to the following formula derived from Poiseuille's law[12]:

$$\frac{1}{R} = \frac{1}{R_1} + \frac{1}{R_2} \ldots + \frac{1}{R_n}$$

Where R = total resistance

$$\left.\begin{matrix} R_1 \\ R_2 \\ R_n \end{matrix}\right\} = \text{respective resistance of each oxygenating unit.}$$

SUMMARY AND CONCLUSIONS

A pressure membrane oxygenator has been described. The oxygen diffusion through a polyethylene membrane 0.00254 cm. (0.001 inch) in thickness, at a pressure of 500 Gm./sq. cm. above atmospheric pressure, was found to be 32.5 ml./M.^{2}/min. and, at a pressure of 1,000 Gm./sq. cm., it was found to be 53.3 ml./M.^{2}/min. This represents increases, respectively, of 427 per cent and 705 per cent in the diffusion efficiency of a similar membrane at atmospheric pressure. In the method described enough blood should circulate around the diffusing membrane to dissolve and combine with all the diffused oxygen in order to prevent the formation of microbubbles. The carbon dioxide elimination was effective and the pH of the blood did not change appreciably.

I wish to express appreciation to Professor Thomas Bridgewood of the Faculty of Engineering, American University of Beirut, for the engineering drawings, and to Mrs. K. Hemadeh for the chemical analysis of the blood specimens.

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CILIARY STREAMING THROUGH THE LARYNX AND TRACHEA

Relation to Direction of Ciliary Beat and Significance in Sites of Respiratory Disease

A. C. Hilding, M.D., Ph.D., Duluth, Minn.

THE PATTERN of flow of the mucous blanket from the bronchial tree through the larynx is so designed as to avoid the squamous epithelium covering the vocal cords.[1] Drainage, on the way to the esophagus, is directed through the interarytenoid area.[2] This region is covered by ciliated epithelium. Lower in the bronchial tree, the *openings of tributary bronchi act as obstructions in the* ciliary stream and these, like the vocal cords, must be bypassed.[3]

Are the curving patterns of flow around these obstructions due to directions of ciliary beat, other than the usual axial one, or, are they due only to unequal, oblique traction upon a tenacious mucous blanket? The present study was undertaken to answer this question. Observations were made of the patterns of flow about the natural obstructions and about artificial obstructions interposed in three different areas: (1) in the trachea, where the ciliary stream flows straight and axial and where the ciliary beat is presumably in the long axis of the air passage; (2) at the carina tracheae where the mucous blanket makes a four-way split and changes direction sharply, and (3) upon the vocal cords, where there is a split of the blanket and a right-angle change of direction.

One cannot avoid wondering if these patterns of flow are related to the distribution of disease in the respiratory tract.

The material used in this study consisted in tracheas removed from freshly killed cows and the larynges and tracheas removed from freshly killed calves.

The specimens were kept, until used, in plastic bags to prevent drying. It was unnecessary to warm the specimens above room temperature to preserve ciliary activity.

The technique was the same as that used in previous studies.[1, 3, 4, 5] The tracheal specimens were split in the midline posteriorly, spread out and nailed or pinned to boards. Some of the laryngeal specimens were similarly split and others were halved by cutting in the midline anteriorly and posteriorly. India ink, placed upon the mucous blanket, was watched in its progress along the ciliary stream.

From the Research Laboratory, St. Luke's Hospital, Duluth, Minn.

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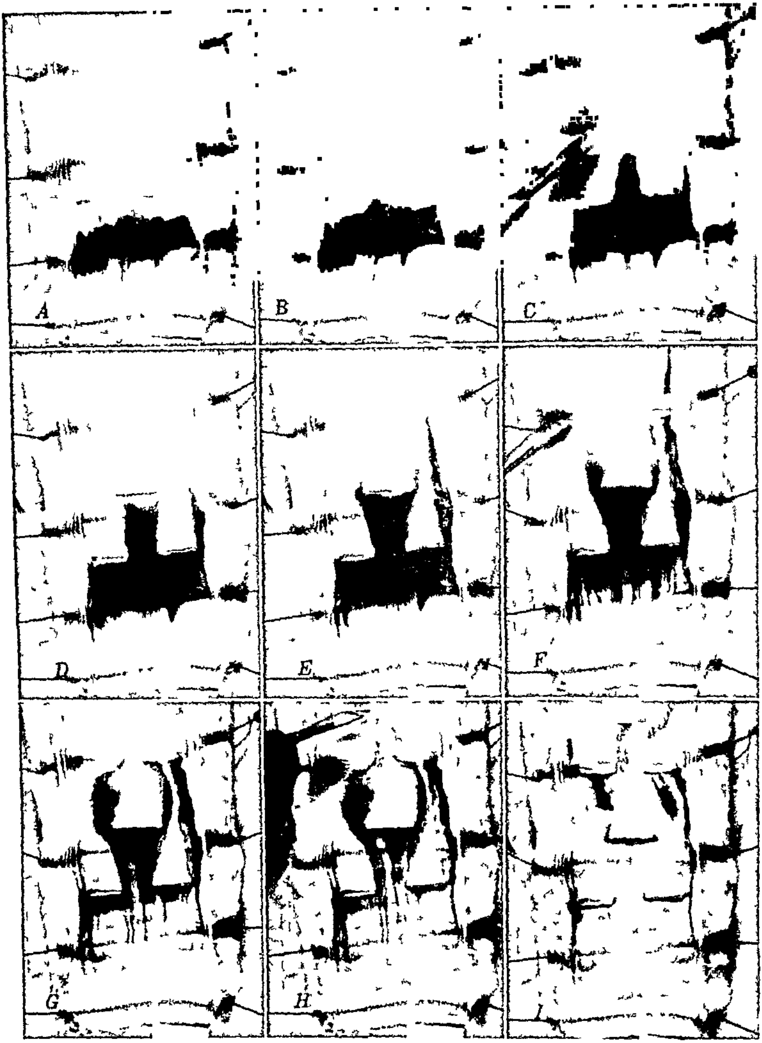

Fig 1 —Trachea of calf showing ciliary streaming about six serially made transverse incisions placed in a pattern The winding course can be readily appreciated by following the central stream through the series This course is presumably due to unequal traction upon the mucous blanket Each incision dividing the blanket removes downstream traction from the area immediately upstream thus reducing the velocity here Three orders of velocity are apparent (1) that of uninterrupted flow (2) that on the upstream side which can be seen by comparing the flow in the right-hand and central streams in *C, D* and *E* and (3) that on the downstream side of the incisions (seen in the right-hand stream in *F* and *G*).

Tracheal Incisions.—Incisions (straight, curved and circular, placed transversely and obliquely) were made through the mucous blanket and mucous membrane in sections of the tracheas of cows in imitation of the natural obstructions, for the purpose of determining the effects of traction upon the mucous blanket and the behavior of the latter at such obstructions.

Transverse: The pattern of flow about single and multiple transverse incisions was found to be rather characteristic, with variations in detail depending upon the viscosity of the blanket and the positions of the incisions relative to one another and to the long axis of the air passage.

It is to be remembered that the ciliary stream in man is upside down. "Downstream" is upward toward the larynx and conversely "upstream" is down toward the alveoli.

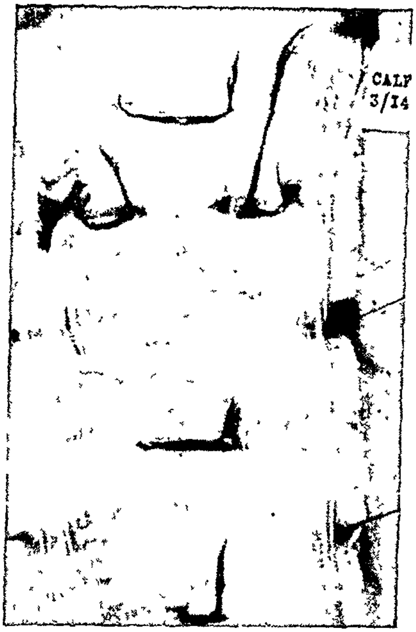

Fig. 2.—Calf trachea showing residual ink-stained mucus pushed into transverse incisions by ciliary action. The second incision from the top was filled to the point where it made contact with the blanket on the downstream side, thus re-establishing drainage.

When India ink is placed upstream from a transverse incision, it flows toward the incision and, at a variable point upstream, some of it begins to deviate toward one or both ends of the incision (Fig. 1). Flow directly toward the incision continues but more slowly than the prongs passing around the ends. The latter may pass the ends of the incision and already be far up the trachea (downstream) before that which is flowing directly toward the incision arrives at its upstream margin. Arriving there, this portion collects and overflows into the incision—a phenomenon that can be explained only by a direct push by the underlying cilia, since the factor of traction at this level has been removed by the division of the mucous blanket. Not infrequently the accumulation in the incision may become so great that it spans the gap, makes contact with the mucous blanket on the downstream side and once more starts off toward the upper trachea (Fig. 2). When the area has cleansed itself of ink, a residuum always remains in the incision.

When a number of incisions are laid out in a pattern, as shown in Fig. 1, the phenomenon of traction and different velocities gives a meandering pattern such as that illustrated. The portions which flow axially are obstructed at the incisions, which they fill more or less completely, and in which a residuum remains when the rest of the mucosa has cleaned itself.

Oblique, inverted "L," and circular incisions: Oblique, inverted "L," and circular incisions were made and the pattern of flow was similar to that described at the transverse incisions, with some variations in detail. In each instance a residuum remained at the upstream margin of the incision.

Axial: Axial incisions did not cause a deviation of flow nor an accumulation of ink. The ink-stained mucus flowed parallel with the incisions on both sides and there was no tendency to overflow the margins.

Curved: Very striking and illuminating were the patterns formed about curved incisions with the concavity directed upstream (Fig. 3). Deviating prongs first flowed past the two horns of the crescents, as past the straight, transverse, or oblique incisions. Later the flow filled in the concavity to the upstream lip of the incision and also the blanket dragged past and over the two horns, as it was pulled downstream by traction.

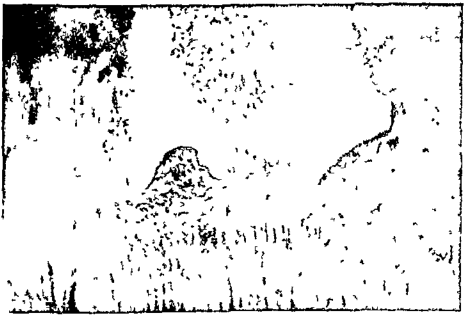

Fig. 3.—Pattern of flow about two curved incisions. Even though the factor of traction has been eliminated within the concavity by the incision, the ink travels to and overflows the upstream margin. This action is due to the ciliary beat.

When the blanket is less viscid, the deviation of flow is less marked. If the blanket is first largely washed away with Ringer's solution, then the flow is almost entirely parallel with the long axis of the trachea and the ink gathers in the incisions with little tendency to flow about the ends. This would seem to indicate that considerable tension may develop in the original mucous blanket under certain circumstances.

Laryngeal Experiments.—The preceding experiments with obstructing incisions in the trachea indicate that, by virtue of traction on the mucous blanket, drainage about obstructions was rather good, even though the ciliary beat was axial in direction. It was not perfect because invariably some residual ink remained at the upstream margin. It is conceivable that drainage about the vocal cords could be explained on the basis of traction alone in the presence of beating cilia in surrounding areas. It would be more effective if the direction of ciliary beat were that of the direction of flow rather than axial. Several experiments were done to determine the direction of beat in the region just inferior (caudad) to the cords.

Axial incisions: In an experiment done on 6 cows and 2 calves, an axial incision was made through the posterior part of the vocal cord and then ink placed low in the anterior larynx or across the entire circumference in the upper trachea or lower larynx. If the ciliary beat had been axial in direction upon the lateral wall and cords, the ciliary flow should then also have been axial in direction, flowing parallel with the incision on both sides, as it did in the trachea; but this it did not do.

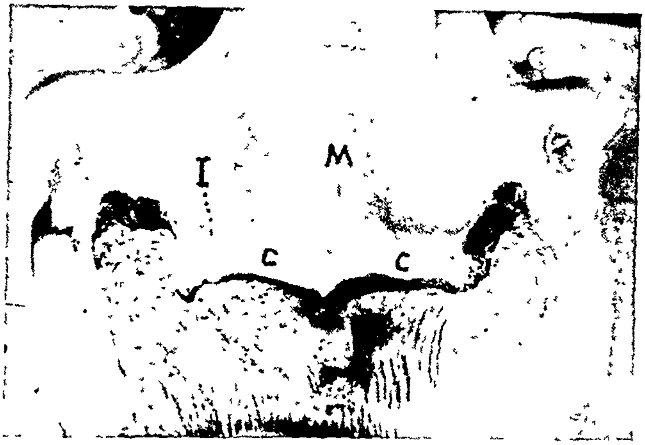

Fig. 4.—Larynx of cow split in midline posteriorly and spread to show the interior. *C* = vocal chords. *M* = Midline anteriorly. *I* = Axial incision across posterior end of vocal cord. This incision eliminated the factor of traction at this line but the oblique directions of flow were not altered indicating that the direction of ciliary beat just below the cords is not axial but oblique.

Four of these larynges were split in the midline posteriorly, spread out and nailed to a board. The incision was made through the mucous blanket and mucous membrane across the arytenoid and posterior part of the left cord. The right side acted as the control (Fig. 4). A line of ink was allowed to flow across the entire circumference of the lower larynx and the larynx placed in an upright position, so that streaming would be upward against gravity. The flow was sluggish in some, but, in general, was about symmetrical on the two sides, flowing up and posteriorly upon the lateral walls to avoid the cords. That upon the anterior half of the left side flowed to the anterior lip of the incision and then overflowed into the incision; that in the posterior half rose posterior to the incision and then flowed away from this in an upward and posterior direction.

Four larynges were divided completely into right and left halves by midline incisions, both anteriorly and posteriorly, and the two halves mounted separately in three and only the left half in the fourth. In 1 (Cow 93), the ink flowed posteriorly and around the inferior end of the incision in the left half. The right was used as a control and showed the usual up and back flow. In another, the flow on the left lateral wall described a spiral course flowing first anteriorly and upward, then swinging posteriorly under the cord to pile up at the anterior margin of the incision (Cow 74). The right half (control) exhibited the same odd anterior, upward and posterior spiral. In the other 2, the flow was up and back to the anterior lip of the incision. In 1 of these (Calf 43), the axial incision was made in both halves. In the right half, the ink-stained mucus filled the incision, made contact with the blanket on the posterior side and was pulled across. Streaming was too sluggish in the left to carry the ink as far as the incision.

These experiments all seemed to show that the posterior flow on the lateral wall of the larynx was *not due to traction* on the blanket because the flow in that direction continued even when the possibility of traction from the interarytenoid area had been removed by the axial incision. Moreover, the fact that ink-stained mucus collected on the anterior lip of the incision, and never the posterior, indicated that the incision lay across the direction of ciliary beat.

Isolation of subglottic region: A rectangle of mucous membrane lying just caudad from the vocal cord was isolated by the axial incision just described and a transverse incision running anterior from this to the midline and parallel with the cord and at the level of the cricoid cartilage. This isolated rectangle was bounded by the midline anteriorly, the axial incision posteriorly, the transverse incision inferiorly, and the squamous epithelium of the cord, superiorly (By ''superior'' is meant cephalad and ''inferior,'' caudad.) Ink was placed at the anterior-inferior corner of the rectangle and its progress observed.

This experiment was done in the larynges of 6 calves. In 5 of these the larynx was split open posteriorly and mounted upon a board with the anterior aspect dependent and the upper end raised somewhat. The left was used as the test side and the right as control. In the sixth, the larynx was completely divided in the midline anteriorly and posteriorly and only the right half used in the test.

In all 6, the direction of flow from the anterior-inferior corner in the isolated rectangle was up and back. Anteriorly it was almost straight up but inclined progressively more and more posteriorly as the arytenoid was approached, until just beneath the arytenoid, it was more back than up. The pattern was symmetrical on both sides but, in some, there was a little more motion on the control side where traction also was effective. Ciliary flow was sluggish in all and, in 3 the ink did not carry as far as the axial incision, but, in the other 3, it flowed to and over the anterior lip of the incision. This experiment also indicates that the ciliary beat in the subglottic region is not axial in direction.

Visualization of Ciliary Beat.—Many attempts were made to visualize the cilia to determine the direction of beat.

Direction of beat in larynx: The wave fronts were seen in a fair number of laryngeal specimens. The wave front ordinarily lies at right angles to the plane of beat and progresses in the direction of beat. The wave fronts in these specimens progressed along curved lines, passing up and back in much the same pattern as the lines of flow.

The left half of the larynx of Cow 124 was irrigated and then stained lightly with India ink. The cilia could be seen fairly well and the direction of ciliary beat just under the cords anteriorly was axial and toward the cord at about right angles but, under the posterior portion of the cords, the direction of beat was posterior and up.

Five hemilarynges from 3 calves were mounted on blocks and chilled in the refrigerator until the cilia slowed and almost stopped. When examined under a dissecting microscope, the direction of beat could be visualized quite readily. A sixth half exhibited such slow ciliary action that the direction of beat could be observed without refrigeration.

In these six hemilarynges, the direction of beat in the subglottic region was axial and toward the cord anteriorly but, progressing toward the arytenoid, inclined more and more backward. Just under the latter it was up and back at about 45 degrees.

Direction of beat in trachea: It has been assumed in these studies that the plane of ciliary beat in the trachea was parallel to the long axis. To verify this, long sections of the tracheas (a third to a half of the full length) from 3 calves were split posteriorly, spread open, mounted on boards and chilled in the refrigerator to slow the ciliary movements sufficiently so that they could be followed. Many fields were examined in each and, with one exception, the beat was parallel to the long axis of the trachea in all 3. In one specimen, in a single field, near the margin of the incision along the posterior wall, where the mucosa was thrown into folds, the beat seemed to be some 15 to 20 degrees off the long axis.

It is conceivable that the direction of ciliary beat might be altered in some way by incisions in the trachea, such as those described above. Therefore, the direction of beat was studied about some of these incisions after chilling and there was no evidence found that the direction had been altered. It remained axial in all fields examined.

DISCUSSION

These studies indicate that the plane in which the tracheal cilia beat is generally parallel with the long axis of the trachea. This, of course, would be expected. Artificial obstructions to ciliary streaming, in the form of variously placed incisions, show no evidence of a change in the direction of ciliary beat.* But the ciliary stream, in these freshly killed cows and calves, deviates more or less to avoid such obstructions, and much of it bypasses. The flow is faster in those portions that deviate than in those that flow directly to the obstructing incision. This would seem to indicate that the blanket in the latter area has been deprived of some of its motivating power, as though there were a downstream pull in the blanket that has been lost by cutting across the blanket.

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*This is consistent with the recently reported findings of Beattie and Correll[6] in reversing a section of trachea while making studies pertinent to a surgical graft of certain portions of the trachea. These workers reversed large sections of trachea in dogs and chickens. They found, as far as the epithelium was concerned, that it all degenerated and disappeared with the exception of islands of replacement cells next to the basement membrane. From these, the epithelium was eventually completely restored by new cells. In the new cells the direction of ciliary beat was the same as that of those lost. In the reversed graft they beat in a caudad direction.

Since the blanket is viscid and will sustain traction, this downstream pull is effective past the ends of the incision and upstream, thus causing the observed deviation. How much, if any, tension develops in the blanket of the normal, living bronchial tree is problematic. How well the blanket would be maneuvered about similar obstructions in the living is unknown. It is known that the nonciliated areas in the nose are drained by traction.

Under certain conditions, the flow of the ciliary stream may be greatly retarded or cease entirely, although the underlying cilia may continue to beat vigorously. Threads of mucus that remain attached within the glands that produced them often extend downstream for considerable distances and are attached to the underside of the mucous blanket. These act as anchors that retard or stop the progress of the blanket even when the cilia continue to beat rapidly.

It could be possible that drainage of mucus about naturally occurring obstructions, such as the bronchial openings, and the vocal cords, is accomplished through traction alone by cilia that beat in an axial direction. This is not the case, however. At both the bronchial openings and the vocal cords, the cilia beat obliquely, to push the blanket past these obstructions. This was demonstrated at the major and minor carinae in a previous study.[5] It was shown to be the case at the vocal cords by the experiments with incisions, as described above, as well as being demonstrated by direct vision after slowing the ciliary beat by chilling. The direction varies between the anterior commissure and the arytenoid cartilage from an axial one at the commissure to an oblique one of about 45 degrees just under the arytenoid.

The epithelium on the margin of the cords is squamous in type, whereas that in the interarytenoid region is ciliated. Practically all mucus normally drained from the lower tract passes out between the arytenoids, the major portion flowing there directly without ever reaching the cords. It is at the cords, however, especially in the anterior portion, that a slowing of drainage takes place. The blanket coming to the anterior commissure and anterior part of the cords approaches at right angles, since the cilia here are beating in an axial plane or nearly so. Here, at the anterior cords, it ceases its axial progress, is torn asunder into two parts, each of which turns at right angles to flow backward under the margin of the cords.

Incomplete studies on human larynges seem to show a pattern like that in these animals inferior to the cord. What it is like above the cords, I cannot say at this time. The bovine animal does not have a ventricle or ventricular band, nor does it have a ventricular appendage, which in man is richly supplied with mucous glands. In man, certain squamous islands often occur in the bronchial tree, especially in the main bronchi. The manner of ciliary flow about these has not been demonstrated but, if traction upon the blanket plays the same role as elsewhere, and it presumably does, then the blanket would flow partly over and partly around such spots with perhaps some retardation of velocity.

One cannot avoid wondering what relation, if any, this pattern of flow has to the distribution of disease in the respiratory tract. Carcinoma occurs most frequently at the margin of the cords and in their ant[illegible] half [illegible]berculous lesions occur characteristically in the interarytenoid area. Why should this difference obtain? I do not think the answer is known, but one is tempted to speculate. Speculation is perhaps permissible as long as one keeps clearly in mind exactly what he is doing.

One possible explanation might be about as follows: An invasion and infection of a spot of tissue by the tubercle bacillus theoretically is a single event. Theoretically, it would be possible for a single organism to initiate a lesion. Since laryngeal lesions are comparatively uncommon in pulmonary tuberculosis, it must be, from the viewpoint of the bacillus, an exceedingly rare occurrence; perhaps it could be compared with the fertilization of the ovum by a sperm cell. This event seems to be purely a matter of chance with a single ovum involved and millions of sperm cells swarming about. This also is a single event. Since practically all of the drainage from the lower respiratory tract passes between the arytenoids, the number of tubercle bacilli passing here would be greater than elsewhere in the larynx, and other factors being equal, the likelihood of invasion would be correspondingly greater—hence the distribution of tuberculous lesions.

As information becomes available concerning the initiation of carcinoma, the indications are that an entirely different process is involved than in the case of the tubercle bacillus. Carcinoma in the larynx is presumably not caused by a single event, rather by the repeated application of certain carcinogenic compounds over long periods of time. The time element plays a big role—not only must the application be repeated a great many times over many years, but each application to a given spot presumably must be of a certain minimal duration. Thus, carcinoma would seem prone to occur at some point where the flow of the ciliary stream, bearing the carcinogenic materials, is retarded more or less. Such an area could be the anterior portions of the cords, where the mucous blanket ceases its axial progress and must be torn in half to pass at right angles in different directions, and this is actually where carcinoma does occur most frequently.

Although the bronchial tree is not the subject of this study, reference has been made to previous studies concerning ciliary streaming and possible modes of carcinogenesis in this portion of the respiratory tract. It might be of interest to point out that carcinoma of the bronchial tree tends to occur in the root of the lungs and that this distribution can be explained on the basis of retardation of ciliary flow. It is in this region that the squamous islands are prone to occur and it is here that numerous large bronchial openings act as obstructions.[3, 4, 7] In the trachea there is usually no obstruction to flow and carcinoma here is infrequent.

CONCLUSION

1. These studies in the larynges of animals indicate that the pattern of ciliary streaming is so designed as to avoid flow across the vocal cords. Eventually practically all of the drainage from the lower tract passes through the interarytenoid region.

2. The observed directions of flow in the larynx are due to a combination of oblique traction upon the mucous blanket and oblique planes of ciliary beat.

3. In the trachea both the ciliary beat and the direction of ciliary streaming seem to be parallel to the long axis of the trachea.

SUMMARY OF SPECULATIVE COMMENT

One can speculate as to the relation these findings might have to the distribution of disease. Tuberculous lesions occur commonly in the interarytenoid area, where the flow of tubercle bacilli reaches its greatest concentration. Theoretically, a tuberculous infection is a single event and, other things being equal, would occur where the concentration of bacteria is the greatest.

On the other hand, carcinogenesis seems to involve many insults of minimal duration repeated frequently over a long period of years. These conditions would prevail where the mucous blanket is retarded in its flow. Such an area would be at the level of the vocal cords, at or near the midline anteriorly, where the mucous blanket ceases its axial progress and is torn asunder to flow at right angles in opposite directions. Actually this is where carcinoma of the larynx is most apt to be found.

Carcinoma of the bronchial tree is prone to occur in the root of the lung, where there are large obstructing openings from tributary bronchi, and where squamous islands are apt to occur. Carcinoma rarely occurs in the trachea where the ciliary streaming is free and uninterrupted.

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THE METABOLIC EFFECTS OF AN INTRATHORACIC STOMACH ON A GROWING CHILD

Theodore C. Jewett, Jr., M.D., David M. Carberry, M.D., and Richard H. Adler, M.D., Buffalo, N. Y.

For many years, surgeons have sought the ideal method for restoring gastroesophageal continuity in extensive lye strictures of the esophagus. Sweet,[11] in 1946, described the technique of subtotal esophagectomy with high intrathoracic esophagogastric anastomosis for the treatment of extensive cicatricial obliteration of the esophagus, which was a major advance over methods previously available. In 1951, Paine[7] reported 2 cases of lye stricture in children who underwent successful esophagogastrostomy. Other reports of similar successes with this operation in infants and children are now comparatively common.

While there has been much discussion as to the possible adverse effects that might occur from an intrathoracic stomach in infants and children, no studies of this nature have been reported in the American medical literature. An intrathoracic stomach is known to be poorly tolerated by the infant during the first 6 months to 1 year of life; thereafter, the problem of acute respiratory distress is of less concern. However, to our knowledge, the effects of a total intrathoracic stomach on growth and development have not been completely documented. Consequently, this paper presents a careful evaluation of the metabolic effects on 2 children with intrathoracic stomachs.

The 2 patients studied were a boy now 13 years of age (M. S.) and a girl now 16 years old (N. H.). Both had intractable lye strictures and underwent esophagectomy with high esophagogastrostomies* 8 years ago.

The cardiorespiratory, hemopoietic, and gastrointestinal systems were evaluated in this study. A careful history and physical examination with special attention to the above-mentioned areas was done, as well as electrocardiogram, pulmonary function studies, chest x-ray, and hematologic work-up.† The gastrointestinal tract was evaluated in relation to the child's growth and development as plotted on the Wetzel Grid.[12] Motility of the intrathoracic stomach was

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From the Department of Surgery, Children's Hospital, Buffalo, and the Department of Surgery, University of Buffalo School of Medicine.

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*Performed by Dr. John R. Paine, Professor of Surgery, University of Buffalo Medical School.

†Hematologic studies were performed by Dr. Clair Shumway, hematologist at Buffalo Children's Hospital.

studied by recording pressures from intragastric tubes and the contour and emptying time of the stomach by barium x-ray studies. Studies included a gastric analysis, Hollander test to determine the presence or absence of vagal innervation. Complete metabolic studies for absorption of carbohydrate, fat, and protein were performed to determine any altered effects due to the intrathoracic stomach.

CARDIORESPIRATORY EVALUATION

Both children had frequent respiratory infections during the first 1 to 2 years following the esophagogastrostomy. Since then, however, this complication has been no more frequent than in normal children. This fact, plus the lack of chronic cough and sputum production, is highly suggestive that there is no postprandial or nocturnal aspiration. Of interest is the persistent presence of dyspnea and fullness in the chest for 1 to 2 hours following the ingestion of larger than normal meals.

Significant physical findings reveal normal contour and expansion of the thorax with no evidence of kyphoscoliosis. Auscultation of the chest was essentially normal. However, musical expiratory râles were noted on occasion in M. S. during episodes of seasonal asthma which this boy has been known to have in the past few years.

The chest roentgenograms were within normal limits. The only abnormality was fullness at the right border of the mediastinum due to the intrathoracic stomach. Electrocardiogram was within normal limits.

Predicted normal pulmonary function cannot be as accurately estimated in children as in adults. However, it is recommended by Ferris and co-workers[1, 2] that these values be based upon age, height, weight, sex, and body surface rather than on only one of these aforementioned factors. The following figures represent the predicted norms of pulmonary function, using Ferris's standards, with the observed values of each child.

Predicted According to:	*Vital Capacity*		*Maximal Breathing Capacity*	
	N. H.	M. S.	N. H.	M. S.
Age	3.27L.	3.48L.	92.0L.	92.0L.
Height	3.41L.	1.82L.	107.3L.	68.0L.
Weight	2.73L.	1.50L.	97.6L.	53.0L.
Body Surface	2.83L.	1.73L.	93.0L.	65.0L.
Observed:	2.60L.	1.37L.	133.0L.	81.0L.

The vital capacity observed in these children fell below predicted normal limits. However, the maximum breathing capacity was well within the normal range. The spirogram pattern of both children showed no abnormalities whatsoever; even the boy (M. S.), who has moderately severe asthma, had no evidence of air trapping. The disparity between the low vital capacity value and the normal maximum breathing capacity is the result of the space-occupying effect of the intrathoracic stomach which lowers the vital capacity. This is particularly significant since these respiratory studies were performed in the fasting state.

HEMATOLOGIC EVALUATION

The results of the hematologic studies on N. H. revealed a normal hemoglobin, hematocrit, white blood cell count, and differential count. The serum iron concentration was 170 gamma per cent. The examination of the blood smear revealed that platelets were present in adequate numbers, and that the erythrocytes exhibited some hypochromia. The alterations of erythrocyte morphology in N. H. were undoubtedly the result of the previous splenectomy done at the time of esophagogastrostomy. Similar studies on M. S. were within normal limits except for an eosinophilia of 19 per cent, which is compatible with his known allergic asthma. The examination of the blood smear revealed that platelets were present in adequate numbers, and that the erythrocytes were normal in appearance.

GASTROINTESTINAL TRACT EVALUATION

After the early compensatory period of 1 to 2 years following the esophagogastrostomy, these children have had relatively normal eating habits. Both of them have excellent appetites and eat three full meals a day and often, after the evening meal, will take a bedtime snack. It is of interest that one of these children (N. H.) can vomit if she so desires; the other child (M. S.) finds that voluntary emesis is impossible even if he so desires. Neither child has had any symptoms suggestive of esophagitis, such as heartburn or substernal pain. M. S. does have some eructation following meals, while N. H. does not. N. H. experiences regurgitation of sour fluid after meals if she lies flat while M. S. does not have this difficulty.

The effects of the thoracic stomach on the growth and development of these children was of major interest (Fig. 1). The growth of these children has been interpolated on to a modification of the Wetzel Grid.[12] The curve of N. H. lies near the median norm both prior to her lye burn and also during the period of esophageal dilatations and gastrostomy feedings. Following her esophageal resection, her growth continued to stay within the area normal for her until the second year following surgery, during which time it slowed rather markedly. This drop can be accounted for by repeated respiratory infections and several bouts of pneumonia during this period. Since then, however, she has had no serious illnesses and her growth curve has return to its previous norm. Today there is no evidence of impairment of growth in this child and the bone age by roentgen examination is likewise normal.

M. S. presents a somewhat more complicated problem. His pre-lye burn and post-lye burn growth area lies within normal limits. However, following his surgery, the curve became subnormal and has remained so, a sign of a definite growth impairment. This is substantiated by the fact that his bone age is also retarded by 2 years. The cause of this impaired growth is somewhat difficult to evaluate, since it could be due not only to the effects of the intrathoracic stomach, but also to the fact that this child is a severe asthmatic during the late summer and fall seasons, which in itself could greatly interfere with his normal growth.

Ingestion of barium by both patients showed normal peristaltic activity on fluoroscopy and complete evacuation of the stomach within 1 hour. It was of interest that a rapid emptying time of the stomach was observed in both patients because only a modified pyloroplasty was performed on M. S. and no pyloroplasty was done on N. H. The intragastric pressure studies were performed by having the subject swallow three fine polyethylene tubes, fused together, which were used to measure pressure from the intrathoracic stomach at the diaphragmatic and midthoracic levels and from the esophagus within the apex of the chest. Pressures from each tube were recorded simultaneously through Statham strain gauges on a multichannel recorder. A lateral hole was made near the distal end of each tube beyond which the tube was filled with mercury to permit its localization by roentgenography. Recordings were made during quiet and deep respirations, coughing, and with manual abdominal pressure in supine and lateral positions. The negative intrathoracic pressure changes were readily transmitted through all three tubes during quiet and deep respirations. Each tube showed positive pressure waves with coughing. Moderate increase in abdominal pressure by manual compression was not reflected through the intrathoracic tubes despite the disturbed anatomy at the diaphragmatic hiatal area from the previous surgery. When the major part of the stomach remains within the abdomen and there is loss of the normal gastroesophageal competence as with hiatus hernia or low supradiaphragmatic esophagogastrostomy, the positive upper abdominal (intragastric) pressure may be [illegible]itted

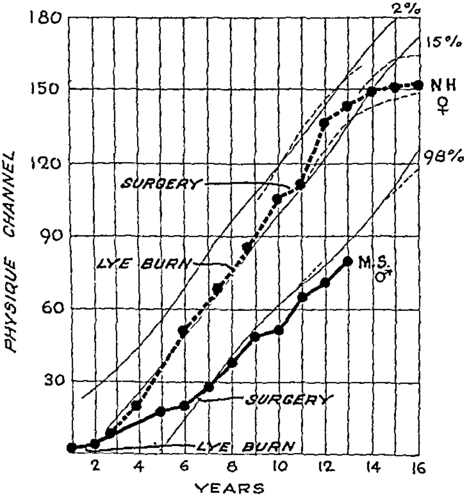

Fig. 1.—Modified Wetzel Grid showing growth and development curves (see text).

to the distal esophagus. At irregular intervals, large positive pressure deflections, apparently from gastric contractions, were recorded from the two intragastric tubes.

Careful evaluation of the position and contour of the intrathoracic stomach using barium contrast medium demonstrated that it lay entirely within the chest in both children. This organ showed a remarkable ability to accommodate over the years to the new position within the thorax. This is illustrated by Fig. 2, which shows a barium study approximately 1 month postoperatively in N. H. and a subsequent study 7 years later. The fundus of the stomach, which once occupied the entire right chest, now lies as a tubular structure adjacent to the mediastinal border.

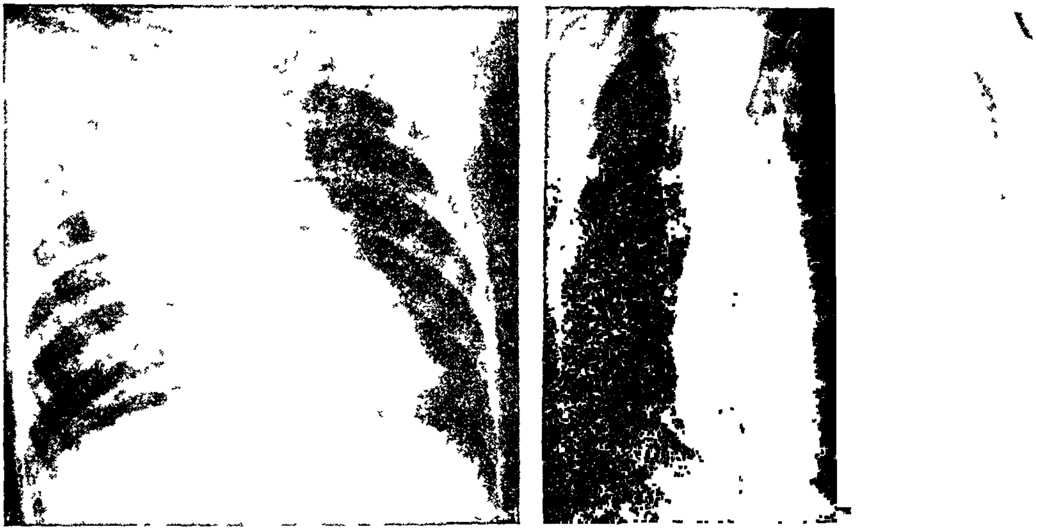
A *B*.

Fig 2.—Barium swallow following high intrathoracic esophagogastrostomy (N H.). *A*, One month postoperative *B*, Seven years postoperative. Note change in contour of stomach.

Because of the altered position of the stomach and the surgical section of the vagus nerves, studies were done to determine the vagal control of gastric secretions and the presence of hydrochloric acid. The two tests used for this purpose were the fractional gastric analysis with histamine stimulation of the stomach and the Hollander insulin test.[4]

The gastric acidity was determined by the method described by Roth and Bockus.[8] This test revealed both children to have free acid and the stomach to respond in a normal fashion to histamine stimulation.

The Hollander test, which was used to determine regeneration of the vagus nerves divided at esophagectomy, showed that there was no response to insulin induced hypoglycemia in either child. This indicates that there is no vagal control over the gastric secretion of hydrochloric acid and that, consequently, no regeneration of the vagal nerve fibers has occurred.

Alterations in carbohydrate, fat, and protein absorption have been described in the literature following gastrectomy or operative procedures which bypass the stomach. No information, however, is available concerning the above-mentioned alterations of absorption in children with thoracic stomach. It was our desire to see if these metabolic functions were disturbed by the total displacement of the stomach from the abdomen to the chest.

The response of the blood glucose level to the oral administration of sugar was utilized as a measure of carbohydrate absorption. After ingestion of a specified amount of glucose, capillary blood sugar levels were taken at regular intervals using the method advocated by Nelson[6] and Somogyi's[10] modifications. Both patients had normal fasting blood sugar levels. Within 30 minutes, there was an extremely high hyperglycemic phase, indicating a surprisingly low tolerance or rapid absorption of carbohydrate (Fig. 3). This type of glucose tolerance curve is often present in gastrectomized patients with the so-called "dumping syndrome" and was believed by Glaessner[3] to be the reason for this symptom complex. Although these children showed this "dumping syndrome" type of glucose tolerance curve, neither child had any of the symptoms commonly associated with this entity. The extremely early high blood sugar levels in these patients are interpreted as being an indication of the rapid and complete transit of the ingested glucose through the stomach, and does not indicate any defect in mucosal absorption.

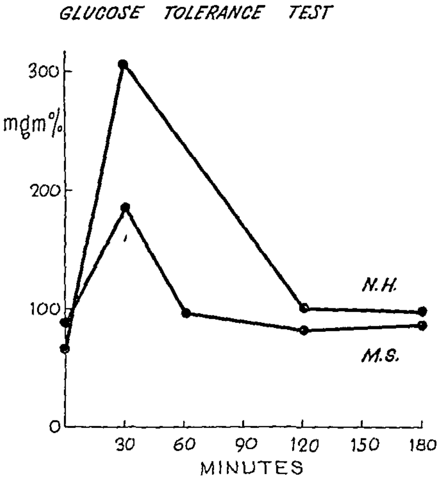

Fig 3.—Glucose tolerance curves (see text).

Although there is no generally accepted adequate test available for fat absorption, the most widely accepted current procedure for a qualitative determination is the Vitamin A tolerance test. The method used in our study was that advocated by May and his colleagues.[5] Both children had extremely flat Vitamin A absorption curves (Fig. 4) which is significant in that this type of curve is noted in most sprue-like syndromes. Since fat metabolism is dependent not only on specific enzyme systems but also on the mechanical efficiency of the gastrointestinal tract, it can be postulated that possibly this defect is the result of incomplete mixing of food materials due to the rapid evacuation from the stomach.

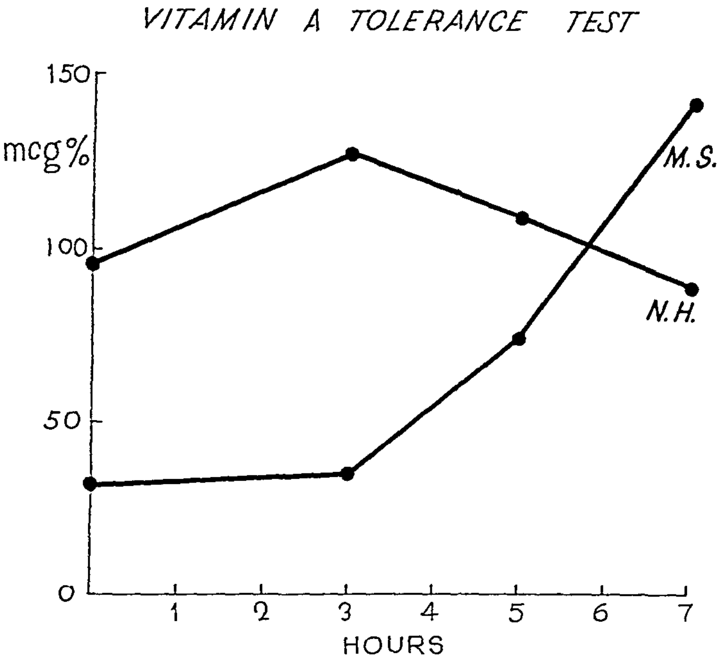

Fig. 4.—Vitamin A absorption curves (see text).

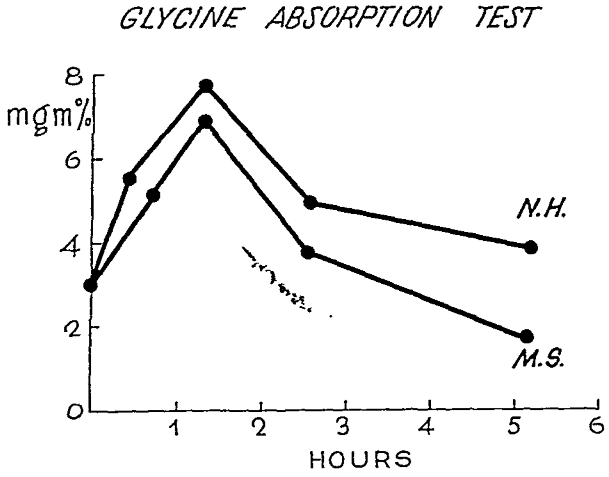

Fig. 5.—Glycine absorption curves (see text).

The ability of the gastrointestinal tract to absorb protein is best studied by determination of one of the specific amino acids rather than the complex protein molecule. The method selected to determine protein absorption was that described by Schwartz and co-workers,[9] in which specific amounts of glycine were ingested and the plasma glycine content then determined. The results of these tests are shown in Fig. 5. Protein absorption is entirely normal in both children.

Electrophoretic determinations of the serum protein fractions were also done. All the elements of the serum protein were within normal limits except for an extremely high gamma globulin level noted on both children. The reasons for this elevated gamma globulin are obscure and its significance is questionable.

DISCUSSION

It is generally agreed by those familiar with the problem that an intrathoracic stomach is poorly tolerated by infants and young children. This impression was certainly confirmed by the clinical course of our 2 patients during their first 2 postoperative years. During this time, they had repeated respiratory infections and moderate dyspnea following large meals; this latter complaint necessitated frequent small meals during the early postoperative period. However, these troublesome complications abated after several years. The manner in which the stomach compensated for these symptoms could be demonstrated by x-ray studies which showed that it changed from a sigmoid-shaped organ into a straightened tubular structure, thus allowing the lungs to have more space in the thoracic cage. While these patients clinically have no evidence of respiratory insufficiency, they have vital capacities which are below the normal for children of similar size, age and sex, but their maximum breathing capacities are normal. This is best explained by the space-occupying effect of the intrathoracic stomach.

Another interesting phenomenon associated with the intrathoracic stomach in these 2 children is the rapid emptying time of the stomach, which is demonstrated by the barium meal and also suggested by the extremely high blood glucose level 30 minutes after ingestion of glucose. This type of curve is characteristically associated with the so-called "dumping syndrome" following gastric resection. It was of interest to us, however, that neither of these children had any of the common symptoms usually seen with the "dumping syndrome." Another alteration of metabolism that was noted was a rather flat Vitamin A absorption curve in both children. The significance of this is not understood, but it can be stated that both children had curves which are seen in states associated with steatorrhea. Possibly this may be related to the rapid transit through the stomach which prevents complete breakdown of food material so that the intestinal enzymes do not have the properly prepared material on which to act. Although food passes rapidly through the stomach, there appear to be no apparent alterations in peristaltic activity. This was observed both on fluoroscopic examinations and also inferred from the intragastric manometric studies.

A definite loss of the cardioesophageal spincter mechanism was confirmed by manometric studies, as might be expected. However, so far there have been no clinical symptoms suggestive of esophagitis, although esophagoscopy is the only way definitely to rule this out. It seems less likely that these children will develop esophagitis from gastroesophageal reflux in the future as long as the stomach continues to empty rapidly and the esophagus is not exposed to acid-pepsin secretions.

The general systemic effects of a thoracic stomach noted by us are somewhat difficult to interpret. One patient, N. H., has perfectly normal growth and development, as shown both by her Wetzel Grid curve and also by bone development. The other child, M. S., has impaired growth both on the Wetzel Grid and by bone age. However, this child also has severe allergic asthma, which may be a contributing cause of his poor growth and development.

SUMMARY

The studies on these 2 children, now 8 years following high intrathoracic esophagogastrostomy for lye strictures, show certain deficiencies previously discussed. The advantages of relieving the tremendous social and economic burden associated with repeated dilatations and gastrostomy feedings by gastroesophageal anastomosis are most gratifying. It would appear that an intrathoracic stomach can be tolerated with only minor disturbances in metabolic functions. Whether this procedure will prove to be a more desirable method when compared with jejunal or colon transplants for re-establishing gastroesophageal continuity awaits the test of time.

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ESOPHAGEAL OBSTRUCTION DUE TO MEDIASTINAL GRANULOMA

Thomas C. Moore, M.D., Muncie, Ind.

THE PRODUCTION of esophageal obstruction by mediastinal granuloma has received scant attention in the literature. Both the rarity of these lesions and the confused state of our knowledge relative to their pathogenesis have contributed to this situation.

The first recorded instance of operation for esophageal obstruction due to a mediastinal granuloma appeared as a case report from the Massachusetts General Hospital in the *New England Journal of Medicine* in 1945.[3] The patient had been operated upon by Dr. Richard H. Sweet. Only 5 additional cases have been recorded up to the present time, 3 of them by Garamella, Stutzman, Varco, and Jensen.[1]

Symptoms of esophageal obstruction were encountered in a minority of the reported cases of mediastinal granuloma collected from the literature in 1955 by Garamella and his associates. Dysphagia had been present in only 6 of the 39 cases of mediastinal granuloma managed by operation which were reviewed by them. Other symptoms encountered in some cases of mediastinal granuloma included dyspnea, cough, chest pain, odynophagia, and fever. Sixteen of the 39 patients had been free of symptoms and had been operated upon because the existence of a more serious type of mediastinal tumor could not be ruled out. Although the number of reported cases is limited, the recording of 16 cases of mediastinal granuloma from the Mayo Clinic by Kunkel and his associates[2] and the recent report of 12 cases from the National Naval Medical Center at Bethesda by Peabody and his associates[6] would seem to indicate that the occurrence of mediastinal granuloma may not be as infrequent as the scarcity of reported cases might suggest.

The etiology of the mediastinal granuloma in the majority of the reported cases has been obscure. In some of the early reports, the lesions were classified as tuberculomas. However, as more cases were recorded, the unsuitability of this classification became increasingly apparent. Tubercle bacilli have seldom been identified in these cases and the bacteriologic yield from the culture of

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From the Surgical Service, Ball Memorial Hospital, Muncie, Ind., and the Department of Surgery, Indiana University School of Medicine, Indianapolis, Ind.

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these granulomas has been uniformly negative. In this regard, it is of considerable interest that Peabody and his associates, in their recent report, found 5 of 12 mediastinal granulomas to be due to histoplasmosis. They found that 2 additional patients had positive skin tests to histoplasmin but that the granulomas removed from these patients were histologically negative for *Histoplasma capsulatum.*

The purpose of this paper is to report a case of esophageal obstruction due to a subcarinal mediastinal granuloma in a 43-year-old woman with symptoms of increasing dysphagia and pain. The patient was managed successfully by extramucosal resection of the granuloma. A patch of fine-mesh nylon was utilized for esophageal support in the area of resection in which only a markedly attenuated mucosal remnant remained to cover the lumen of the esophagus.

CASE REPORT

The patient, a 43-year-old white housewife, was admitted to the Ball Memorial Hospital on April 27, 1955, because of difficulty with swallowing and recent roentgen demonstration (as an outpatient) of esophageal obstruction. She had noticed increasing difficulty with swallowing during the 4 weeks prior to her admission to the hospital. Her swallowing difficulties were accompanied at times by a feeling of substernal fullness and back pain. Initially her troubles were limited to the ingestion of solid foods. However, by the time of her admission to the hospital, she was also experiencing difficulty with liquids. On April 16, roentgen study of the esophagus with orally ingested barium had been carried out. A small diverticulum was demonstrated on the right lateral wall of the middle portion of the esophagus. The diverticulum measured approximately 1 cm. in diameter and emptied readily. About 2 inches below the diverticulum, in the subcarinal area, a nonopaque, ovoid filling defect in the esophagus was identified (Fig. 1). Thick barium was retained at this level. There was no esophageal dilatation above this area of partial obstruction. The mucosal pattern of the esophagus did not appear to be disturbed by the obstructing mass.

The patient had been healthy throughout her life up to the onset of her present illness. There was no history of exposure to tuberculosis. The findings on physical examination were essentially within normal limits. The admission red blood count was 5.1 million with 16.5 grams of hemoglobin. Her white blood count was 6,200 with a differential count of 2 per cent eosinophils, 2 per cent basophils, 40 per cent lymphocytes, 9 per cent monocytes, and 47 per cent neutrophils. The urine examination was within normal limits. Two days following her admission to the hospital, the roentgen study of her esophagus with barium was repeated. The findings confirmed the observations made 13 days earlier. There was no change in the appearance of the esophageal obstruction. On April 30, esophagoscopy was carried out. The lumen of the esophagus appeared to be completely obstructed at the approximate level of the radiologically demonstrated obstruction. The esophageal mucosa which covered the obstructing mass was intact and appeared to be normal. No effort was made to biopsy this mass through the intact esophageal mucosa or to thrust the esophagoscope past the obstructing mass. On the basis of the esophagoscopic and roentgen findings, a tentative diagnosis of benign extramucosal esophageal tumor, most likely leiomyoma, was made.

On May 2, the patient was taken to the operating room and a right lateral thoracotomy was carried out under general, endotracheal anesthesia through the bed of the resected sixth rib. The small diverticulum on the right lateral wall of the middle portion of the esophagus was identified. In the subcarinal area, between the esophagus and the right main bronchus, an oval, almost egg-shaped, mass in the wall of the esophagus was encountered. The mass was relatively large in comparison to the size of the esophagus at this level and measured approximately 3 by 2 cm. The mass was solid and clearly encroached upon the lumen of the esophagus. A small portion of this tumor was excised for frozen section microscopic study. The examining pathologist reported that the tissue appeared to be granulomatous rather than neoplastic. The mass had a yellowish appearance on section and was of a firm consistency. It was easily separated from the adjacent normal tissue from which it was sharply demarcated. The mass appeared to have replaced not only the outer muscular layers but a substantial portion of the submucosa and adjacent inner layers as well. The mass was completely removed without entering the lumen of the esophagus. A rather large defect in the wall of the esophagus remained. Throughout the area of this defect, the lumen of the esophagus was covered only by a filmy, tissue-paper thin layer of epithelium and some adjacent lamina propria remnants. It was apparent this defect in the wall of the esophagus, covered as it was only by a thin membrane, could not be left without additional external support. It was feared that approximation of the remaining muscle layers and adjacent submucosa would produce too much constriction in the esophageal lumen at this point. Because of encouraging experience in the laboratory during this period with the use of nylon mesh in the support and repair of experimentally created abdominal wall defects, the use of nylon mesh to support the esophagus in the area of this defect was decided upon.[5] An oval patch of nylon mesh was sutured to the muscle and submucosal layers at the margins of the defect with multiple interrupted sutures of 4-0 silk. The nylon mesh was from the same bolt of material which was used with success in the repair of the abdominal wall defects in the laboratory. It contained 270 by 204 threads per square inch. The thoracotomy incision was closed in layers and a catheter which was left in the chest during closure was aspirated and withdrawn.

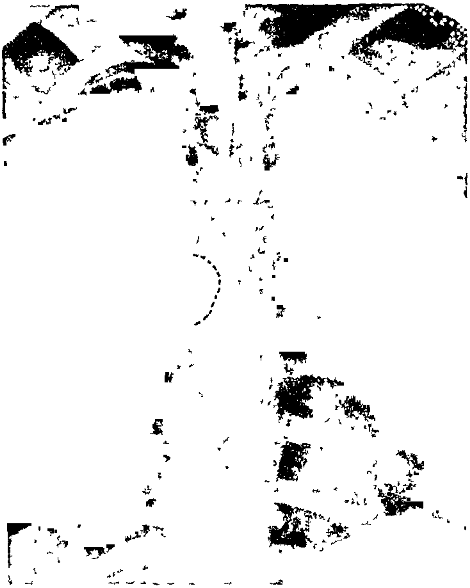

Fig 1 —Roentgenogram illustrating esophageal obstruction by extraluminal mass (*dotted line*).

On microscopic examination, the tumor was found to be a chronic granulomatous mass with many histiocytes and small numbers of multinucleated giant cells (Fig. 2). Sudan III stain revealed the presence of fat globules in many of the histiocytes. Examination with both the periodic acid-Schiff stain and the Bauer stain failed to reveal the presence of Histoplasma. Tubercle bacilli were not seen.

The patient did well following operation. Gastric suction was maintained for 3 days by means of a nasogastric tube which had been passed into the stomach at the time of operation. Her postoperative course was complicated only by the development of a superficial wound abscess which was satisfactorily managed by drainage. She has experienced no further difficulty with swallowing in the 3 years which have passed since her operation.

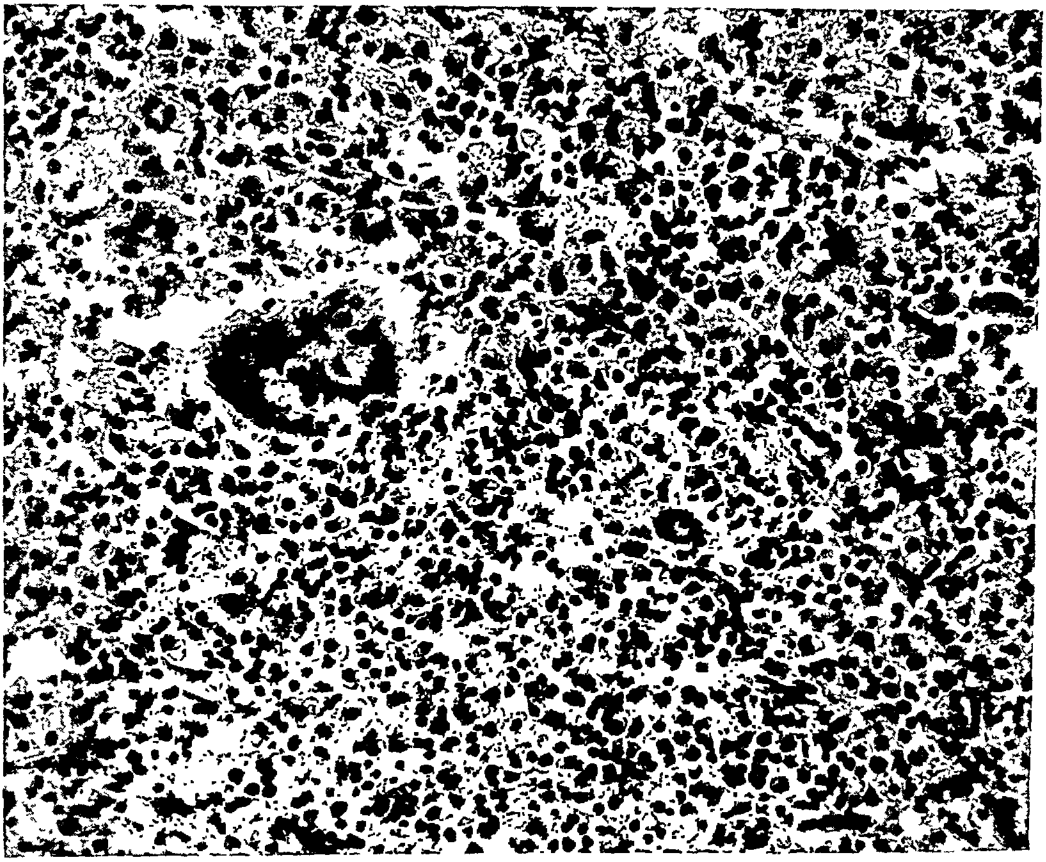

Fig. 2.—Photomicrograph of a section of the resected mass revealing a rather characteristic granulomatous appearance with multinucleated giant cells.

A recent roentgen study of the esophagus with barium, nearly 3 years following operation, showed no evidence of esophageal obstruction, narrowing, or other abnormality. The mucosal pattern of the esophagus appeared to be normal throughout.

Skin testing for sensitivity to tuberculin and histoplasmin was carried out 3 years following operation. The patient was found to have a 4 plus reaction to tuberculin and a 3 plus reaction to histoplasmin.

DISCUSSION

A review of the clinical findings in the 7 recorded cases of surgically managed, symptomatic esophageal obstruction due to mediastinal granuloma, including the case recorded here, reveals that all of the patients were between the ages of 24 and 43 years (Table I) Five of the 7 patients were females Dysphagia occurred in all of the patients and was accompanied by chest pain or pain on swallowing in all The duration of symptoms ranged from 3 weeks to 1 year

Roentgen study of the esophagus with barium was carried out in 5 patients In all of them the roentgen studies were interpreted as indicating the presence of an extrinsic, extraluminal mass which was producing esophageal obstruction Dilatation of the esophagus above the point of obstruction was not observed and the mucosa was found to be intact over the obstructing mass in all 5 cases

Esophagoscopy was carried out in 4 of the 7 patients The obstruction was found to be extraluminal and the mucosa intact in all of them No attempts were made to biopsy the obstructing mass through the intact mucosa One examination, that reported by Samson and Dugan,[8] was complicated by esophageal perforation and the development of a mediastinitis

Preoperative skin tests with tuberculin and histoplasmin were obtained in 2 patients A 1 plus reaction to tuberculin and a 2 plus reaction to histoplasmin were observed in the first case of Garamella and his associates, while both reactions were negative in their third case In the case recorded here, skin test reaction to tuberculin 3 years following operation was 4 plus and that to histoplasmin was 3 plus A few acid fast bacilli could be identified in a smear from the resected granuloma in only 1 of the 5 patients upon whose granulomas this study was carried out Culture and guinea pig inoculation of material from this granuloma were negative for tuberculosis Culture and inoculation studies were negative in all 4 of the granulomas investigated by these techniques

The mediastinal location of the granuloma in these cases with esophageal obstruction is of considerable interest The granuloma was reported to be subcarinal in 5 of the 7 cases In 1 case, the mass was found in the posterior superior mediastinum, adherent to the right side of the trachea It was located between the trachea and the esophagus In the case report from the Massachusetts General Hospital, the only cited localization of the mass, at the carina, was based on the roentgen study In 4 of the cases, the mass was reported at operation to be located between the right main bronchus and the esophagus These findings suggest that a degree of the esophageal obstruction in these cases may have resulted from the trapping of the esophagus, by the expanding granulomatous mass, between the rigid posterior chest wall and the relatively rigid tracheobronchial tree, with its resulting compression The mediastinal granuloma was subcarinal in 4 of the 39 cases reviewed by Garamella and his associates and esophageal obstruction with dysphagia was found in all 4

All 7 of the patients were managed by resection of the granuloma and all recovered In 2 of the patients, reported by Garamella and his associates, an unspecified area of submucosa was left bare by the resection These muscular defects in the esophagus were stated to have been repaired in both cases In the case reported by the author, the granuloma had destroyed not only the muscle layer of the esophageal wall but a portion of the submucosa and adjacent

TABLE I. SUMMARY OF REPORTED EXPERIENCE WITH ESOPHAGEAL OBSTRUCTION DUE TO MEDIASTINAL GRANULOMA

CASE NO.	AUTHOR	YEAR	AGE	SEX	SYMPTOMS	DURATION OF SYMPTOMS	MEDIASTINAL LOCATION OF GRANULOMA	OPERATION	RESULT	REMARKS
1.	Case report of Mass. Gen. Hosp.[3] Case 31341	1945	43	F	Dysphagia, pain	6 weeks	At carina	Excision of granuloma	Recovered	Location of mass from roentgen study; anatomic location of mass at operation *not given*
2.	Samson, et al.[7] Case 1	1950	27	F	Dysphagia, pain	12 months	Right posterior superior	Excision of granuloma	Recovered	Mass adherent to right side of trachea and located between trachea and esophagus
3.	Samson and Dugan.[8] Case 2	1951	29	F	Dysphagia, pain	3 months	Right subcarinal	Excision of granuloma	Recovered	
4.	Garamella, et al.[1] Case 1	1955	24	M	Dysphagia, pain	5 months	Right subcarinal	Excision of granuloma*	Recovered	Mass between right main bronchus and esophagus
5.	Garamella, et al. Case 2	1955	39	F	Dysphagia, pain	10 weeks	Right subcarinal	Excision of granuloma*	Recovered	Mass between right main bronchus and esophagus
6.	Garamella, et al. Case 3	1955	25	M	Dysphagia, pain	3 weeks	Right subcarinal	Excision of granuloma	Recovered	Mass between right main bronchus and esophagus
7.	Moore	1958	43	F	Dysphagia, pain	1 month	Right subcarinal	Excision of granuloma; nylon mesh support of esophageal defect	Recovered	Mass between right main bronchus and esophagus

*Area of submucosa left bare by excision. Muscle defect repaired.

outer mucosal layer as well. Although the granuloma was excised without entering the lumen of the esophagus, the mucosal remnant left covering the esophageal lumen was much too insubstantial to be left without additional support. Because of the size of the defect, it was feared that approximation of the adjacent intact walls of the esophagus would produce too much narrowing of the lumen of the esophagus. The use of a patch of fine-mesh nylon was decided upon to provide the needed support because of the successful experience of the author and Siderys,[5] at this time, with this material in the experimental repair of abdominal wall defects in animals. The nylon patch appeared to have been tolerated well despite the prior presence in the repaired area of a granulomatous mass. Recent experimental studies in dogs have shown nylon mesh patches to be tolerated satisfactorily in the wall of the esophagus.[4]

SUMMARY

1. The literature pertaining to mediastinal granulomas, especially those granulomas which produce symptomatic esophageal obstruction, is reviewed.

2. A case of esophageal obstruction in a 43-year-old woman with increasing dysphagia and pain, due to a subcarinal mediastinal granuloma, is reported. The patient was managed successfully by resection of the granuloma and the use of a patch of fine-mesh nylon for support in the area of resulting esophageal wall weakness.

3. The reported experience in 7 operatively treated cases of symptomatic esophageal obstruction, due to mediastinal granuloma, is analyzed.

4. The dysphagia was found to be accompanied by chest pain or pain on swallowing and these symptoms were often of increasing severity.

5. The mediastinal granulomas which produced symptoms of esophageal obstruction tended to occur most frequently in the subcarinal area. It is surmised that the obstruction in these cases may have resulted from the compressing effect of an expanding granulomatous mass in this relatively unyielding area between the rigid posterior chest wall and the somewhat less rigid, but structurally firm, tracheobronchial tree. Mediastinal granulomas in other areas rarely produced symptoms of esophageal obstruction.

6. The bacteriologic and histologic studies carried out in these cases were of little assistance in establishing the pathogenesis of these granulomas. A more vigorous search for the possible presence of histoplasmosis, by skin testing and special histologic study of the granuloma, is urged in future cases.

7. In patients with symptomatic esophageal obstruction due to an extraluminal mass in the subcarinal area, associated with pain, the diagnosis of mediastinal granuloma should be strongly considered.

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SEGMENTAL RESECTION FOR PULMONARY TUBERCULOSIS

An Analysis of 335 Cases

Viking Olov Björk, M.D., Upsala, Sweden

Segmental resection, made possible through the advent of antimicrobial therapy, is today an established and accepted procedure in the surgical treatment of pulmonary tuberculosis. The rate of sputum conversion has been found to be high and the morbidity and mortality rates are low. One of the greatest values of segmental resection is its preservation of pulmonary function.

Patients with a very limited pulmonary function have been accepted for segmental resection, e.g., resection of two segments and one subsegment on the only remaining left lung, following a previous pneumonectomy. Of 335 patients, 12 are dead and 170 have been restudied. Ninety-one patients were excluded, as the observation time was less than 1 year. Fifty-eight patients have refused re-investigation, mainly because they did not like to have another bronchospirometry. Of these, many are well and working full time but it has not been possible to obtain a personal restudy. Four patients from abroad are well and working but have not had postoperative lung-function tests. About half of the patients (47 per cent) had bilateral tuberculosis. The extent of the tuberculosis in the contralateral lung is shown in Table I. Seven patients had an open cavity in the contralateral lung. Sixty-one patients had had a cavity in the contralateral lung closed at the time of surgery: in 40 cases by a pneumothorax, in 17 by a thoracoplasty, and in 4 cases by conservative measures. In 17 per cent of the cases, it was necessary to do an extrapleural resection with a decortication of the remaining lung.

From the Thoracic Surgical Clinic, University Hospital, Upsala, Sweden.
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TABLE I. THE CONDITION OF THE CONTRALATERAL LUNG AT THE TIME OF OPERATION

CONDITION OF THE CONTRALATERAL LUNG	NUMBER OF CASES
Normal	175
Old pleurisy	5
Small infiltration	67
Infiltration earlier treated by pneumothorax	15
Cavity "closed" by conservative treatment including chemotherapy	4
Cavity "closed" by pneumothorax	40
Cavity "closed" by thoracoplasty	17
Open cavity	4
Open cavity under pneumothorax or thoracoplasty	3
Segmental resection	3
Decortication and pneumonectomy	2
Total	335

Age is not in itself a contraindication for segmental resection in cavitary tuberculosis. The oldest patient, a 64-year-old man, tolerated well a segmental resection of the apical segment of the right upper lobe and a small thoracoplasty in one stage. Five years after operation he is in good condition and has negative guinea pig tests of the sputum and gastric washings. The reason for adding a thoracoplasty in this aged patient was emphysema and fibrosis of the remaining lung. The other 4 patients above the age of 60 also survived the operation.

The postoperative course must be carefully supervised in these older patients. Perfusion of blood through nonventilated areas of lung will decrease the arterial oxygen saturation, causing symptoms of coronary insufficiency. Whenever there is an insufficient ventilation in the postoperative course which cannot be immediately improved by more conservative measures, a tracheostomy with prolonged artificial ventilation should be instituted to guarantee the patient a normal oxygen and carbon dioxide tension.

Eight patients were operated on under the age of 20, the youngest being 9 years. In 6 of these young patients, no space-diminishing procedure was needed. In 1, an extrapleural pneumothorax space was developed at the end of the resection and filled with air to diminish the intrapleural space after the operation. In 1 patient, the diaphragm was mobilized around its periphery and resutured at a higher level. This latter operation is not recommended for general use as it results in impaired lung function. However, in the young and growing patients under the age of 20, it may occasionally be the best space-diminishing procedure. In the above case, there was 25 per cent of oxygen uptake on the left side after the procedure. The ventilation, however, was only 11 per cent. The age and sex distribution are shown in Table II and Fig. 1.

The indications for segmental resection are as follows: (1) tuberculous cavitation in 314 cases (94 per cent), (2) bronchiectasis with positive sputum in 5 cases, (3) bronchial stenosis in 2 cases, (4) tuberculous empyema with bronchial fistula in 2 cases, and (5) tuberculoma in 12 cases.

Preoperative Investigation of Pulmonary Function.—The most important information of pulmonary function is obtained by a study of all x-ray films from the beginning of the disease. The maximal movements of each diaphragm

TABLE II AGE AND SEX DISTRIBUTION IN 335 PATIENTS UNDERGOING SEGMENTAL RESECTION FOR PULMONARY TUBERCULOSIS

AGE	MEN	WOMEN	TOTAL
0 9	1	—	1
10 19	3	4	7
20 29	33	42	75
30 39	69	46	115
40 49	70	29	99
50 59	28	5	33
60 69	3	2	5
Totals	207	128	335

is also recorded When a segmental resection is intended, it is extremely important to examine frontal as well as lateral tomograms as pointed out by Chamberlain and Klopstock[3] The maximal breathing capacity and on certain indications a bronchospirometry should be performed before the operation

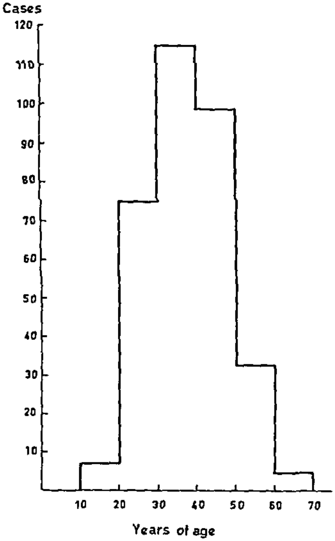

Fig 1—The age distribution in 335 cases of segmental resections for pulmonary tuberculosis

Mortality—Twelve patients died (Fig 2) The operative mortality was 1 5 per cent The cause of death in 3 patients was ventilatory insufficiency One 59 year old woman, with bilateral cavitary tuberculosis died 2 days after operation in spite of artificial ventilation by respirator through a tracheostomy One 41-year old man had had a tuberculous cavity in the right lung treated by pneumothorax for 6 years That treatment had resulted in a right sided fibrothorax There was a 10 year history of cavitary tuberculosis in the left lung treated for 5 years by pneumothorax After the left sided pneumothorax was abandoned, there were two cavities, one in the upper lobe, and one in the superior segment of the lower lobe. In this patient, the apicoposterior segment of the left upper lobe, as well as the superior segment of the left lower lobe, were resected and at the same time an osteoplastic thoracoplasty was performed. Because of the thickened pleura over the right lung, the thoracoplasty and the extensive resection of the left lung, it was necessary to do a tracheostomy on the third day to add artificial respiration by respirator. This artificial respiration was needed for 8 days, after which the patient made an uneventful recovery. One month after operation a pulmonary edema developed, and he died suddenly. Autopsy showed lipoid degeneration of the myocardium, and right-heart insufficiency with failure and stasis. The third patient, who died from ventilatory insufficiency, was a 38-year-old man who had had a seven-rib thoracoplasty on the right side 6 years earlier. A resection of the apicoposterior segment of the left upper lobe plus a wedge of left lower lobe was performed for cavitary tuberculosis. On the fifteenth day after operation he went into coma and arterial puncture showed a carbon dioxide tension of 124 mm. Hg, and an oxygen tension of 42 mm. Hg. Tracheostomy was performed but it was too late. Before

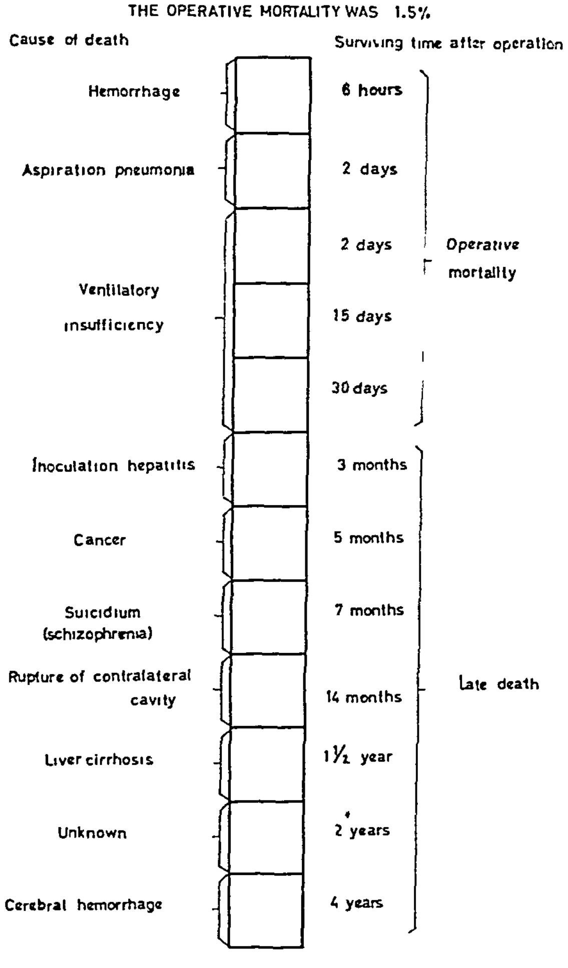

Fig. 2.—The operative mortality was 1.5 per cent (5 cases). There were 7 late deaths.

operation, bronchospirometry showed a 72 per cent oxygen uptake on the left side. Cardiac catheterization, however, showed a pressure in the pulmonary artery of only 17 mm Hg; after occlusion of the left pulmonary artery it rose to 32 mm Hg mean pressure and after occlusion of the right main pulmonary artery plus work, the mean pressure in the pulmonary artery rose further to 45 mm Hg, with a systolic peak of 64. That patient had a maximal breathing capacity of 49 L per minute preoperatively. Today such a patient would have been treated immediately after operation by tracheostomy and by artificial ventilation for at least 1 week. One patient died from hemorrhage, despite 13 units of blood by transfusion.

One 30 year old patient, who 5 years earlier had had an extrapleural pneumothorax on the left side for cavitary tuberculosis, underwent resection of the posterior segment of the right upper lobe. After operation she vomited and died of an aspiration pneumonia.

Seven other patients in this series have died since operation. The causes of death included cirrhosis, carcinoma, hepatitis, suicide, cerebral hemorrhage, and 1 patient died following rupture of a tuberculous cavity on the right side 14 months after a segmental resection on the left. A 44 year old man died 2 years after operation from an unknown cause.

Complications.—Nonfatal complications occurred in 15 per cent of cases of segmental resection.

1. *Air leakage* was the most important complication after segmental resection and occurred in 10 per cent of the patients. Leakage occurred more frequently if either a decortication had been done for an old pneumothorax or if there had been an atypical resection, either wedge resection or subsegmental resection. Of these patients 7.5 per cent were treated by closed drainage. In 2.5 per cent it was necessary to add further surgery, i.e., a thoracoplasty in 1 case, a thoracoplasty with decortication in another case, and in 2 cases it was necessary to do a resection with lobectomy plus chest wall extirpation. There were 2 cases of empyema. One healed by closed suction; in the other patient there was a downhill course with progression of disease in both lungs.

2. *Accidental opening of a tuberculous cavity* occurred in 3 cases without any late complication.

3. *Wound infection* was encountered in 3 cases but healed with chemotherapy.

4. *Ventilatory insufficiency* was encountered in 6 cases. In 2 patients a tracheostomy was performed; in 4 additional cases, it was necessary to add artificial ventilation by a respirator. This treatment was continued from 1 to 21 days.

5. *Trauma to the big vessels*. In 1 case, an incision was accidentally made in the subclavian artery during the course of an osteoplastic thoracoplasty. The incision was closed by vascular suture. In 2 cases the pulmonary artery was injured and in both cases repaired.

6. *Postoperative pain* radiating out in the arm was encountered in 1 patient who had had resection of the apicoposterior and anterior segments of the left upper lobe plus an osteoplastic roof-thoracoplasty, leaving the first rib in place. Thus, a scalenus anticus syndrome was produced and the patient was reoperated upon half a year later with resection of the first rib, after which the symptoms disappeared.

7. *Spillover with infiltrations in the contralateral lung* occurred in 1 case. Tracheostomy had to be performed and artificial ventilation with respirator was needed for 3 days, after which the patient made an uneventful recovery.

There were no postoperative complications in 85 per cent of the patients undergoing segmental resection for pulmonary tuberculosis.

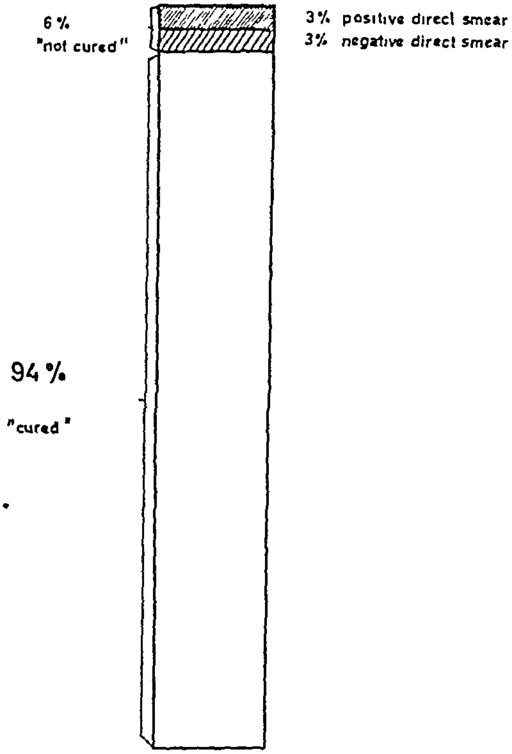

Fig. 3.—Ninety-four per cent were considered "cured." Only 3 per cent were positive on direct smear.

RESULTS

A patient was considered "cured" if (1) there was a negative guinea pig test on gastric washing and sputum, as well as negative cultures on sputum and a negative direct smear, on 3 consecutive days, and (2) no active disease was found at an x-ray examination. All these criteria were fulfilled in 160 patients of 170 patients restudied (94 per cent) (Fig. 3).

Of the 10 patients "not cured," 4 had a positive direct smear. This was due to reactivation on the contralateral side in 3 cases, and on the same side as the resection in 1 case. Five patients were negative on direct smear, but had a positive guinea pig test Four of these were working full time, and one performed a half day's work Of the 5 patients who had positive guinea pig tests on gastric washings, 1 had a pneumothorax for cavitary disease on the contralateral side, 1 had a contralateral, extrapleural pneumothorax for cavitary disease, and a third patient had contralateral *calcified pulmonary infiltration* as well as bronchiectasis The last patient in the group of those not cured was negative on direct smear and on guinea pig test of gastric washings, but had a positive culture of the sputum She was working full time 6 years after operation, was free of symptoms, had a normal sedimentation rate, but x ray studies showed some infiltration at the site of resection

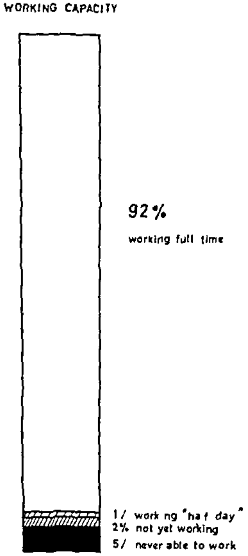

Fig 4—*The working capacity*

Working Capacity (Fig 4)—Of 158 "cured" patients, 146, or 92 per cent, were working full time 1 year after the operation Many different professions were represented, of which housework and office work were most frequently encountered Two patients performed a half day's work and 10 did not work at all Of these, 6 patients were considered unable to take up work again Of these, 5 had had extensive bilateral tuberculosis with a maximal *breathing capacity varying from 32 L up to 70 L per minute* One had a contralateral pneumothorax, 2 had contralateral 7 rib thoracoplasties, and 1 a 5 rib thoracoplasty The remaining patient had gone through segmental resection without a thoracoplasty, but due to rheumatic arthritis in both shoulders she was unable to perform any work at all

The arm movements were recorded and compared in 4 different groups of patients (Fig. 5). In a small group of 4 patients who had had a mobilization of the diaphragm as a space-diminishing procedure, there were normal arm movements in all. Pain following resection varied with the procedure (Fig. 6).

In the small group of 4 patients who had mobilization of the diaphragm as a space-diminishing procedure there were no complaints of pain.

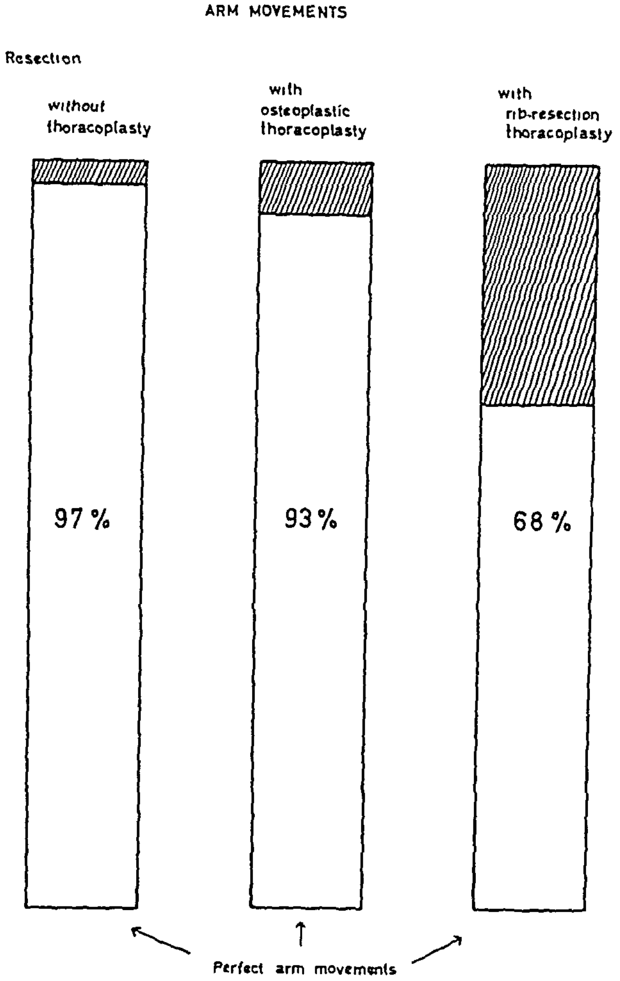

Fig. 5.—The best cosmetic and functional result regarding the arm movements was naturally found in patients undergoing resection without thoracoplasty. If a thoracoplasty was needed, the result was far better if an osteoplastic thoracoplasty was added than if a thoracoplasty by rib resection was performed.

Cough.—Seventy-four per cent of the patients did not have any cough at the time of restudy. The remaining 26 per cent experienced some irritating cough, usually called the smoker's cough, or they had some expectoration in the morning. In a few patients, suture granulomas were found around silk stitches, which had to be removed through the bronchoscope. In order to avoid this complication, it is the author's policy to use 30-day chromic catgut on atraumatic needles for bronchial closure and bronchotracheal anastomosis. This technique seems to be especially important in cases of pulmonary tuberculosis. A suture granuloma may cause a positive guinea pig test which turns negative after removal of the suture These suture granulomas have been proved to contain tuberculous tissue

Dyspnea —Eighty per cent of the patients did not feel any shortness of breath The 20 per cent who complained of dyspnea were usually cases of far advanced bilateral disease

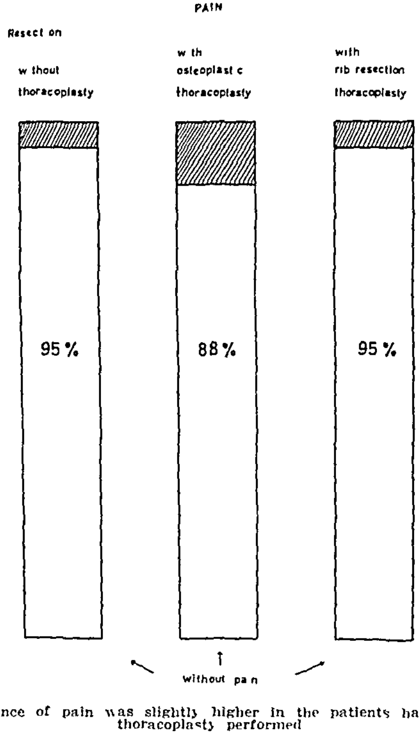

Fig 6 —The incidence of pain was slightly higher in the patients having an osteoplastic thoracoplasty performed

Functional Results (Figs 8 and 9) —When the material is analyzed in order to find out the loss of function after the various segmental resections only unilateral cases have been included It is obvious that parenchymal and pleural disease on the contralateral side will give a false bronchospirometric result For instance, 1 patient showed a left sided oxygen uptake of 60 per cent before and 53 per cent after resection of apicoposterior segments of the left upper lobe and an osteoplastic thoracoplasty due to pleural disease on the contralateral side

Wedge resection can be performed without any significant loss of function. However, even the smallest resection may cause some impairment of function due to the fixation of diaphragm following most thoracotomies, in spite of breathing exercise. The more anatomic subsegmental resection is preferable to a wedge resection, in order to avoid dividing the drainage bronchus too close to the tuberculous lesion. A tuberculous endobronchitis in the divided little bronchus once caused infection and a fistula necessitating re-resection.

If one segment was removed the maximal breathing capacity decreased by 22 L. to 109 in male patients and by 16 L. to 77 in female patients.

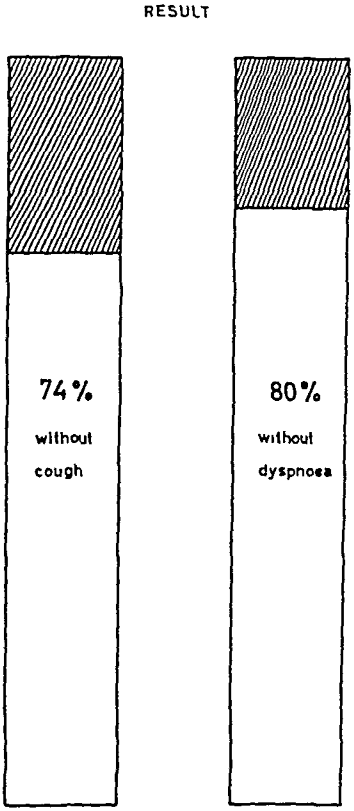

Fig. 7.—Twenty-six per cent of the patients had cough at the follow-up and 20 per cent were short of breath.

The maximal breathing capacity diminished 12 L. to 83 L. per minute in male patients undergoing resection of one segment with additional thoracoplasty. In those patients operated upon on the right side, the diaphragmatic movement was on an average 4.8 cm. as compared to 5.7 cm. on the left side.

Resection of one segment always causes some decrease of function on the operated side. When the resection is performed without thoracoplasty only a very slight decrease of oxygen uptake and ventilation is encountered. When a thoracoplasty is added there is a further decrease in oxygen uptake on the operated side although the ventilation remains approximately the same.

Resection of an additional subsegment to one segment did not cause any further reduction in pulmonary function.

Resection of 2 segments caused a decrease in the maximal breathing capacity of 26 L. to an average of 100 L. per minute in men (10 cases) and of 19 L. to 97 L. per minute in women (3 cases). If an osteoplastic thoracoplasty was added to the resection of 2 segments, there was a decrease of 23 L. to 94 L. per minute in men (5 cases). The addition of a thoracoplasty with rib resection in 3 men caused a decrease of 13 L. to 85 L. per minute.

The maximal diaphragmatic movements after resection of 2 segments on the right side was on an average 4.4 cm. on the right and 5.8 cm. on the left side (8 cases). After a left-sided resection, the maximal movements of the diaphragm were 4.8 cm. on the right as compared to 4.0 cm. on the left side (4 cases). If an osteoplastic thoracoplasty was added to a right-sided resection of 2 segments, the diaphragmatic excursion was measured to an average of 5.9 cm. on both right and left sides in 7 cases. In 6 cases of a similar left-sided procedure, the right diaphragm moved 5.5 and the left 5.0 cm. (6 cases). Addition of a thoracoplasty with rib resection to resection of 2 segments on the left side resulted in a movement of 5 cm. on the right and 3.5 cm. on the left side in 2 cases.

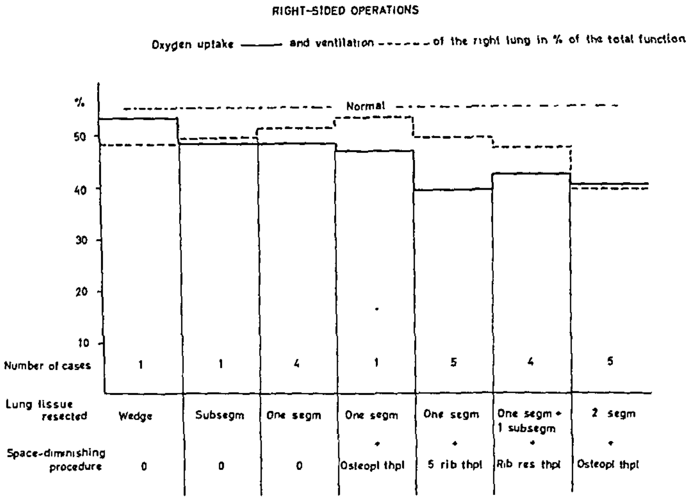

Fig 8.—Diagram of the oxygen uptake and ventilation of the right lung in per cent of the total function after segmental resections on the right side. The segmental resection without thoracoplasty gives hardly any reduction in ventilation or oxygen uptake. Combined with thoracoplasty there is some reduction of oxygen uptake as well as of ventilation; however, the remaining lung function after these operations has been very good indeed.

The oxygen uptake and ventilation are only slightly decreased after resection of 2 segments. If a thoracoplasty was added, either an osteoplastic type or by rib resection, a significant decrease in both oxygen uptake and ventilation was observed.

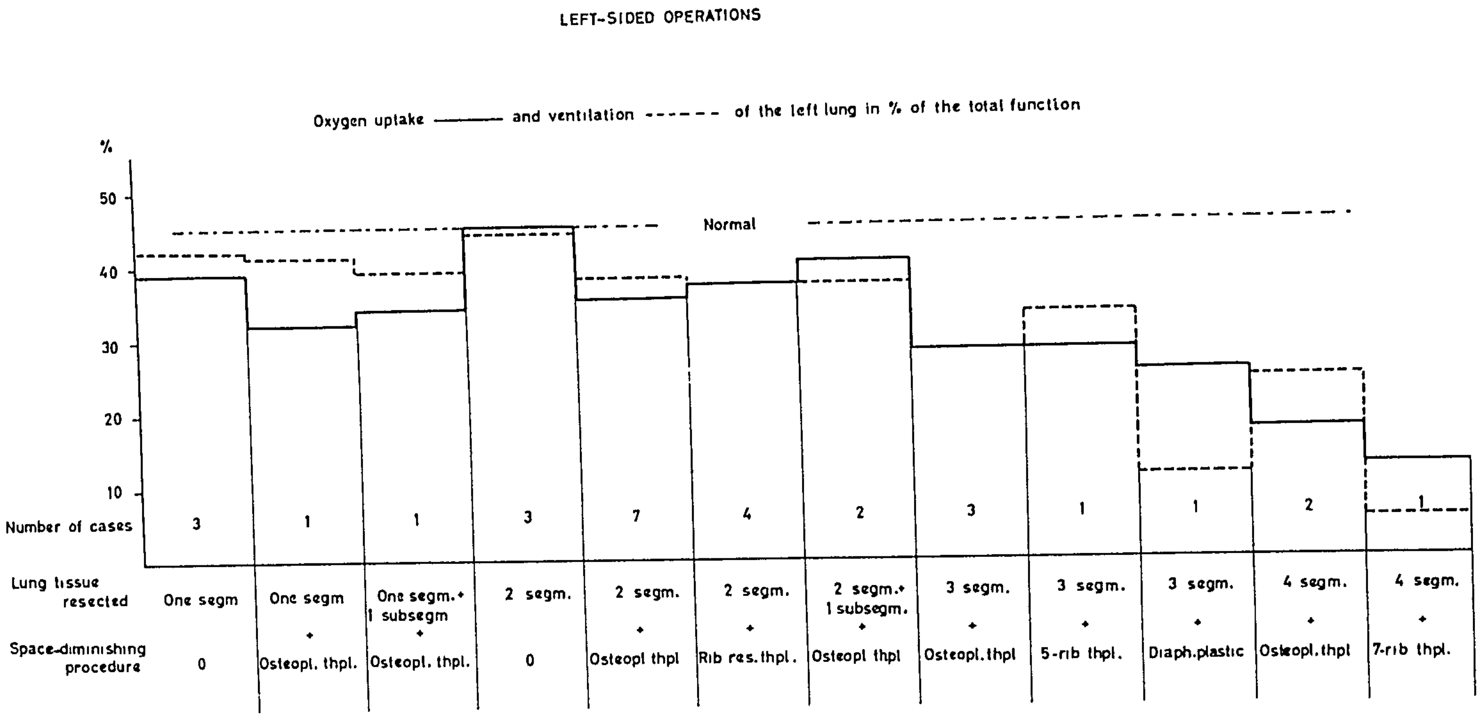

Fig. 9.—Diagram of the oxygen uptake and ventilation of the left lung in per cent of the total function after segmental resections on the left side. For resection of up to 2 segments there is only an insignificant reduction of function of the operated side. If more lung tissue is resected the impairment of lung function is correspondingly increased.

Resection of 3 segments and a thoracoplasty caused a decrease in the maximal breathing capacity of 42 L. to 91 L. per minute in 5 cases.

After resection of 3 segments with a space diminishing procedure, there was a significant decrease of oxygen uptake and ventilation on the operated side. Different space diminishing procedures did not influence the oxygen uptake, but the ventilation was most decreased in the patient having a mobilization of the diaphragm.

Resection of 4 segments with an osteoplastic thoracoplasty caused a marked drop in oxygen uptake and in ventilation on the operated side (Figs. 8 and 9).

SUMMARY

An analysis is made of 335 cases of segmental resection for pulmonary tuberculosis. The operative mortality (including patients with marked ventilatory insufficiency) was 1.5 per cent. Of the 170 patients followed from 1 to 6 years, it has been gratifying to find 97 per cent with a negative direct smear and 94 per cent with a negative culture and guinea pig test of sputum and gastric washings. Ninety-two per cent were working full time. The incidence of impaired arm movements, pain, cough and dyspnea is recorded. The best cosmetic result and best arm movements were obtained when no thoracoplasty was added. The diaphragm mobilization gave the best cosmetic but the worst functional result of the different space diminishing procedures. The osteoplastic thoracoplasty gave a better cosmetic result and better arm movements when compared with a thoracoplasty with rib resection. There was a higher incidence of postoperative pain in the group in which rib resection thoracoplasty was performed. The late functional result has been very encouraging and it has been proved that segmental resections can be performed with a minimal loss of function. The contralateral side has withstood the resection very well.

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AN ANALYSIS OF THE PULMONARY FUNCTION OF NINETY PATIENTS FOLLOWING PNEUMONECTOMY FOR PULMONARY TUBERCULOSIS

G. J. Tammeling, M.D., and C. D. Laros, M.D., Appelscha, The Netherlands*

SINCE it has become evident that special cases of pulmonary tuberculosis can be treated adequately by pneumonectomy, several authors have published data concerning the influence of this operation on pulmonary function.[2, 4, 5, 7-11, 13-15]

From the functional point of view, the consideration as to whether a pneumonectomy is justifiable or not depends on both the results of the preoperative function tests and of the expected changes of the function of the remaining lung in the early and late postoperative period. An analysis of the results of these tests in patients who underwent a pneumonectomy several years ago is, therefore, of special importance in determining which patients can be treated in the future by pneumonectomy without risks with respect to pulmonary function.

From various publications, it is clear that, in most patients, distention of the lung tissue in the postoperative period occurs. It could not be proved, however, that distention resulted in pulmonary emphysema.[5, 7, 8, 9, 14] With regard to the interpretation of distention after pneumonectomy, opinions differ. Most authors consider distention as an unfavorable condition with respect to the pulmonary function.[2, 5, 15, 16] Cournand[5] and Birath[2] and their associates regarded pulmonary distention as a condition in which the ventilatory capacity is limited and the respiratory efficiency is reduced. Rienhoff,[14] on the other hand, interpreted distention as a physiologic phenomenon and regarded any method employed to impede this dilatation as unprofitable.

The performance of a thoracoplasty, with the intention of facilitating the adaptation of the remaining lung to the modified intrathoracic conditions, is considered undesirable by most authors.[7, 8, 9, 11] Rossier and Bühlmann[15, 16] on the contrary, hold the view that the best results are obtained by preventing the distention as much as possible. They state that the combination of pneumonectomy and thoracoplasty ("Deckplastik") always leads to a striking increase of the ventilatory economy, even in patients with a pre-existing thoracoplasty.

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*From the Sanatorium "Beatrixoord" at Appelscha, The Netherlands; Director: Prof. J. K. Kraan, M.D. Present address: St. Antonius Hospital, Utrecht, The Netherlands.

The purpose of this paper is to discuss the results of the pulmonary function tests in a group of 90 tuberculous patients at an average period of 52 months after pneumonectomy and to compare these results with those published by other authors.

MATERIAL

The patients examined belonged to a group of 125 patients in whom Eerland[10] and co-workers performed a pneumonectomy for pulmonary tuberculosis in the years between 1947 and 1954. At the time of the follow-up study, 105 patients were alive. As of December, 1956, 90 patients submitted voluntarily to a follow-up study of their pulmonary function. The function of 4 additional patients was studied after this date. Eleven patients refused. Of the 90 patients, the functional data just before the pneumonectomy, at the time of the discharge from the hospital and those at the time of the follow-up study were available. The time interval between operation and discharge ranged from 5 to 30 months (mean 11 months), whereas the time between operation and follow-up study ranged from 29 to 84 months (mean 52 months).

In Table I the age groups for each of the sexes at the time of the operation and at the follow-up are given. The average age at the time of the pneumonectomy was 30 years and 8 months, at the follow-up 35 years.

TABLE I. AGE OF PATIENTS BEFORE PNEUMONECTOMY (BP) AND AT THE TIME OF FOLLOW-UP EXAMINATION (FU)

AGE GROUPS IN YEARS	FEMALE		MALE		TOTAL	
	BP	FU	BP	FU	BP	FU
15-19	6	1	2	—	8	1
20-29	15	11	19	7	34	18
30-39	21	24	20	24	41	48
40-49	2	7	4	10	6	17
50-59	—	1	1	5	1	6
Total	44	44	46	46	90	90

The final period of treatment previous to the operation averaged 59 months and the mean interval between the discovery of the tuberculosis and the pneumonectomy was 103 months. In most of the cases, an illness of long duration preceded the operation and, in spite of prolonged bed rest and many forms of drug therapy or active treatment, slow progression took place not uncommonly leading to total destruction of the tissue of one of the lungs.

In Table II, the roentgenologic status of both the resected and the contralateral lung at the time of pneumonectomy is given. At the time of the follow-up, the clinical status of 87 patients was good while, in 3 cases, the tuberculous lesions were not yet fully cured.

The analysis of the function data of the 90 patients is hampered by the multitude of factors which can be active. We have explored 5 of these: (1) sex, (2) whether remaining lung is right or left, (3) the presence or

TABLE II. THE ROENTGENOLOGIC LESIONS IN THE LUNGS AT THE TIME OF THE PNEUMONECTOMY

RESECTED LUNG	CONTRALATERAL LUNG				TOTAL
	NO LESIONS	INDURATIVE LESIONS			
		MINIMAL	MODERATE	EXTENSIVE	
Destroyed	11	16	7	1	35
Empyema	6	4	4	3	17
Extensive lesions	9	10	4	—	23
Moderate lesions	4	6	3	—	13
Minimal lesions	2	—	—	—	2
Total	32	36	18	4	90

absence of thoracoplasty, (4) asthmatic symptoms, and (5) diaphragmatic paralysis (Table III).

TABLE III. DISTRIBUTION OF THE 90 PATIENTS IN FIVE PAIRS OF FACTORS INFLUENCING THE PULMONARY FUNCTION

PAIRS OF FACTORS		♂	♀	Rr	Lr	Ta	Tp	Aa	Ap	Pa	Pp
Male patients	♂	*46*	—	30	16	19	27	30	16	39	7
Female patients	♀	—	*44*	31	13	33	11	27	17	34	10
Remaining right lung	Rr	30	31	*61*	—	35	26	43	18	52	9
Remaining left lung	Lr	16	13	—	*29*	17	12	14	15	21	8
Thoracoplasty absent	Tp	19	33	35	17	*52*	—	33	19	35	17
Thoracoplasty present	Ta	27	11	26	12	—	*38*	24	14	38	0
Asthmatic factors absent	Aa	30	27	43	14	33	24	*57*	—	47	10
Asthmatic factors present	Ap	16	17	18	15	19	14	—	*33*	26	7
Diaphragmatic paralysis absent	Pa	39	34	52	21	35	38	47	26	*73*	—
Diaphragmatic paralysis present	Pp	7	10	9	8	17	0	10	7	—	*17*

Thoracoplasty was not performed in 52 patients (Group I) and was done in 38 (Group II). In 27 patients of Group II, the thoracoplasty was performed before the pneumonectomy. In most of these patients, thoracoplasty was done because resection therapy was not yet available. Very active forms of tuberculosis and empyema—both frequently combined with drug resistance—formed the remaining indications. Thoracoplasty before or during the pneumonectomy was only done for empyema. The extent of the thoracoplasty varied from 4 to 10 ribs, as follows:

Number of ribs partly resected	4	5	6	7	8	9	10.
Number of patients	12	2	3	7	7	1	6

In Figs. 1-8, asthmatic patients are pointed out by the use of a segment of a circle below the circle itself. The distribution of asthmatic patients in Groups I and II is almost equal (Table III).

METHODS

For the spirometric recordings, the spirometer designed by Dirken and Orie* was used.[17] All measurements were performed with the patients in the supine position. The volumes are given at ATPS.†

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*Manufactured by Lode N. V., Groningen, The Netherlands.

†Ambient temperature and pressure saturated with water vapor.

The vital capacity was determined by measuring the maximum volume inspired after a complete expiration The VC* was measured in triplicate and the highest value was regarded to be the best one

The timed vital capacity in one second was measured according to the technique of Tiffeneau[18] The TVC was determined at least in quadruplicate and the highest value obtained was taken for the calculations The TVC is not only expressed as a percentage of the VC—TVC/VC ratio—but also as a percentage of the TLC—TVC/TLC ratio—for a reason explained later

The total lung capacity was obtained by adding the residual volume to the vital capacity

The maximum breathing capacity was measured at 30 breaths per minute This frequency was indicated by the examiner In the case of a slight difference in that frequency, the values were corrected This technique has the following advantages (a) 30 breaths per minute is for most patients the optimum breathing frequency during exercise (b) the data are reproducible and have a better mutual comparability, (c) the FRC during hyperventilation (MBC) is accessible to mutual comparison, and the MBC can be compared with the predicted MBC, which can be calculated from the TVC by multiplying it by 30 ($MBC_{predicted} = 30 \times TVC$)

Before the operation and at the time of discharge of the patients, the FRC was measured by a closed system method At the resting respiratory level, the patients were connected with a spirometer system of known volume, filled with nearly pure oxygen By mixing this oxygen with the gas in the lungs, the oxygen concentration in the system decreased and the extent of the fall is a measure for the volume of the gas in the lungs at the moment of the connection to the spirometer system During the whole determination the volume of the lung spirometer system was kept nearly constant by compensating the oxygen uptake of the patient The gas analysis was performed by measuring continuously the change of the thermal conductivity of the gases

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*The following abbreviations are used in this paper

TLC = total lung capacity in milliliters
VC = vital capacity in milliliters
TVC = timed vital capacity or volume expired during the forced vital capacity maneuver in the first second in milliliters
FRC = functional residual capacity in milliliters
FRC^r = FRC in rest
FRC^h = FRC during hyperventilation
RV = residual volume in milliliters
ERV = expiratory reserve volume in milliliters
MBC = maximum breathing capacity in liters
RV/TLC = ratio of RV to the TLC in per cent
FRC/TLC = ratio of FRC to the TLC in per cent
TVC/TLC = ratio of TVC to the TLC in per cent
TVC/VC = ratio of TVC to the VC in per cent
bp = value before the pneumonectomy
ad = value at the discharge from the sanatorium
fu = value at the time of the follow up study
VC_{br} = the VC of the contralateral lung before the operation as calculated from the VC_{bp} and its bronchospirometrically found percentage

in the spirometer by means of a diaferometer.*[20] At the follow-up study the FRC was measured by an improved closed circuit method using helium—2.8 per cent in room air—as an indicator gas.[12, 17, 21] A detailed description of this method is given elsewhere.[17] In only 12 patients was the FRC at the follow-up examination determined by the original technique.† Since, in the original technique, no correction was made for the nitrogen elimination from the blood, the values obtained by the modified technique were somewhat smaller—about 10 per cent.[17] The values of the FRC are the mean values of determinations in duplicate, in such a way that only differences less than 200 ml. were accepted.

The FRC during hyperventilation—FRC^h—was obtained by adding the change of the expiratory level, which may occur during the performance of the MBC, to the FRC in rest—FRC^r. A rise of the expiratory level results in an increase of the FRC, and a shift of the level to the expiratory side results in a decrease in the FRC.

The residual volume was obtained by subtracting the expiratory reserve volume from the FRC^r ($RV = FRC^r - ERV$).

Bronchospirometry was performed preoperatively in 61 patients. In most cases, the Carlens catheter and the McKesson double spirometer, filled with oxygen, was used. Since 1954, the Lode double spirometer is used. Before 1950, bronchospirometry was performed with the Zavod catheter.

The normal values for the VC are calculated according to Anthony from the tables of Harris and Benedict for basal metabolism.[1] In the statistical treatment of the material, the various standard errors (S.E.) and the correlation coefficient (r) are calculated with the methods indicated by Bradford Hill.[3] If two means or two proportions differed by more than twice the value of the standard error of the difference, the difference is said to be "significant." In the instances when it was three times its standard error, it was said to be "highly significant." $p = 0.05$ is taken as level of significance; S_r = the standard error of the correlation coefficient.

RESULTS

The Vital Capacity.—

1. An impression of the changes in the VC as a result of the removal of the affected lung is obtained by comparing the VC_{bp} (before pneumonectomy) with the VC_{fu} (follow-up). In Fig. 1 the VC_{bp} is plotted against the VC_{fu} for each patient. The points falling at the right of the line $VC_{bp} = VC_{fu}$ indicate patients with a greater VC at the follow-up than before the operation, those falling at the left indicate the reverse situation. In 87 per cent of the cases, the VC_{fu} was smaller than the VC_{bp}.

2. In the same way, as in Fig. 1, a comparison is made between the VC_{fu} and the VC_{br} (Fig. 2). In this graph, the data of only 61 patients are given,

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*Manufactured by Kipp N. V., Delft, The Netherlands.

†In 12 patients, the function tests were performed in the Department of pulmonary diseases of the State University at Groningen. Chief: Prof. N. G. M. Orie, M.D.

owing to the fact that bronchospirometry was not performed before the operation in every case In 67 per cent of the patients without a thoracoplasty (Group I), the VC_{fu} exceeded the VC_{br}, while this occurred in only 29 per cent of the cases with a thoracoplasty (Group II) This difference between the two groups proved to be statistically highly significant (S E 0 131, difference 0 394) The mean values of the VC_{fu} and the VC_{br} of these 61 patients

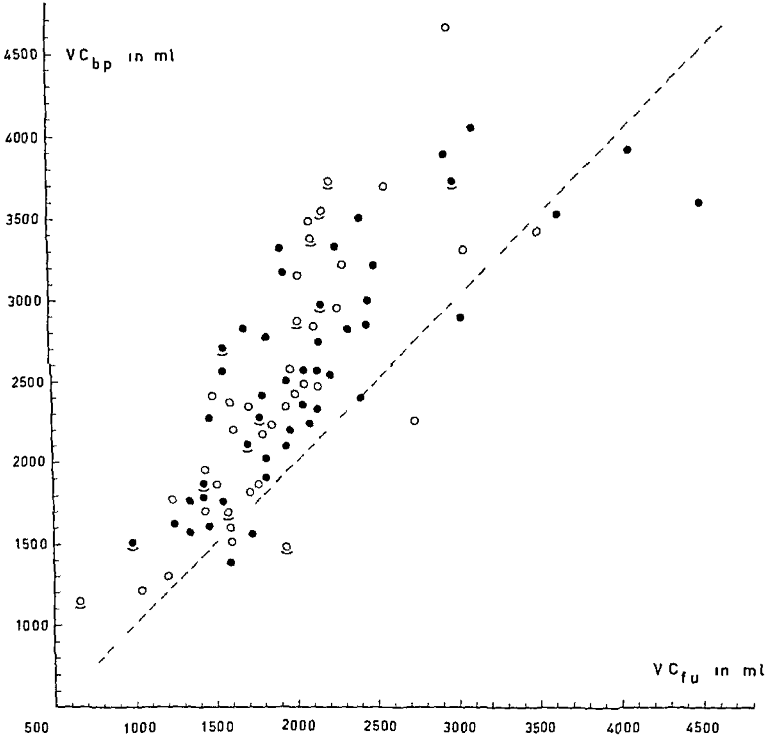

Fig. 1—Comparison of the VC before the pneumonectomy (VC_{bp}) and at the follow up (VC_{fu})
● Patients without a thoracoplasty (Group I)
○ Patients with a thoracoplasty (Group II)
∪ Patients with asthmatic symptoms

are given in Table IV These data suggest that the decrease of the VC of the contralateral lung in Group II is due mainly to the values of the patients who underwent a thoracoplasty after the pneumonectomy

3 In Table V, the 61 patients of Table IV are divided into three equal groups, according to the extent in which the resected lung took part in the

TABLE IV. THE MEAN VALUES OF THE VITAL CAPACITY OF THE REMAINING LUNG IN MILLILITERS

	GROUP I	GROUP II			TOTAL
			THORACOPLASTY BEFORE AND AFTER PNEUMONECTOMY		
	40 PERSONS	21 PERSONS	15 PERSONS (BEFORE)	6 PERSONS (AFTER)	61 PERSONS
Calculated according to Anthony[1]	1,740	1,900	1,880	1,940	1,800
VC_{br}	1,970	2,060	1,990	2,210	2,000
VC_{fu}	2,130	1,970	1,970	1,970	2,070

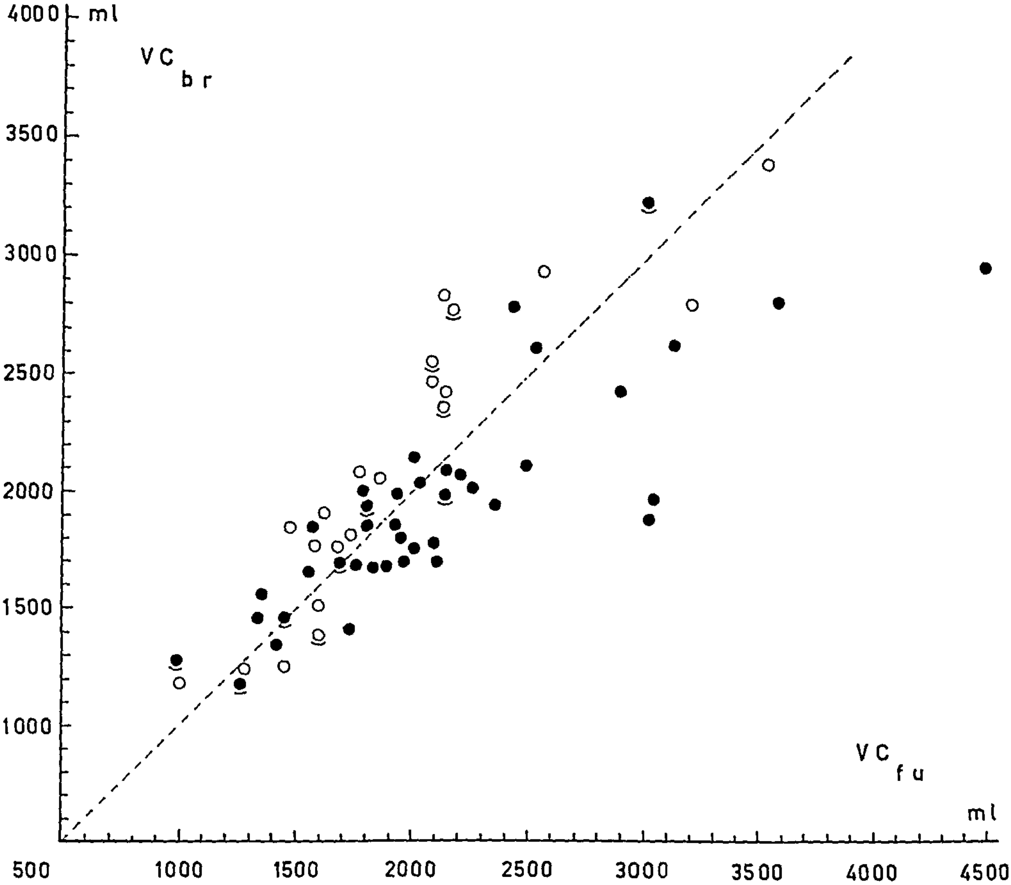

Fig. 2.—Comparison of the VC of the remaining lung before the pneumonectomy (VC_{br}) and at the follow-up (VC_{fu}).

VC_{bp}. By comparing the percentages of expected and actual loss of the VC in these groups, the following conclusions can be drawn: (a) In the group with a mean expected loss of 6 per cent, the actual loss was significantly higher ($p = 0.001$). In this group of 21 patients, 11 had a thoracoplasty before or during the pneumonectomy and, in 3 patients, a thoracoplasty was performed after the pneumonectomy. (b) In the group in which the participation of the resected lung ranged between 15 and 26 per cent, the expected loss corresponds with the actual loss. (c) In the group with the mean expected loss of 34 per cent, the actual loss is significantly smaller ($p = 0.01$). In the latter two

TABLE V. THE RELATION BETWEEN THE MEAN EXPECTED LOSS (VC_{bp} - VC_{br}) AND THE MEAN ACTUAL LOSS (VC_{bp} - VC_{fu})

NUMBER OF CASES	PARTICIPATION OF THE RESECTED LUNG IN THE VC_{bp}	MEAN EXPECTED LOSS AS PER CENT OF THE VC_{bp}	MEAN ACTUAL LOSS AS PER CENT OF THE VC_{bp}
21	0-14%	6%	16%
20	15-26%	20%	19%
20	27-45%	34%	26%

groups (b and c), there were only three and four thoracoplasties, respectively; 6 before or during the pneumonectomy and only one after the resection.

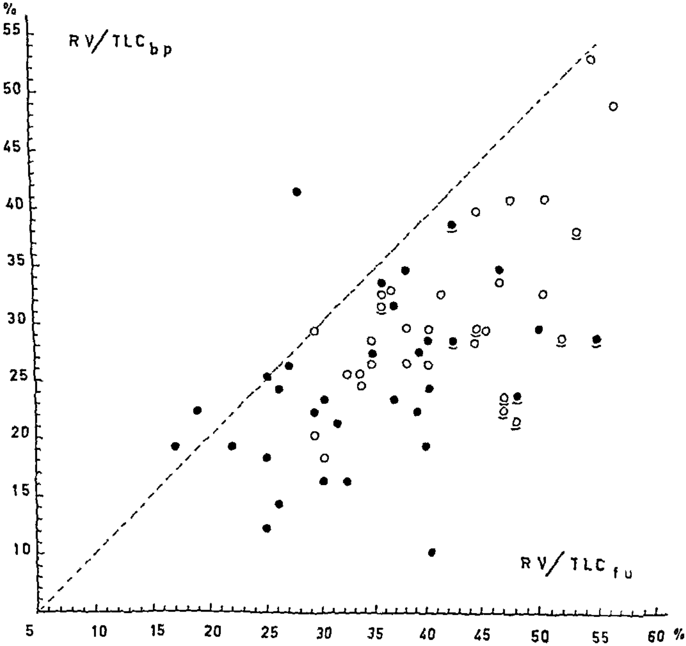

Fig. 3—Comparison of the RV as a percentage of the TLC before the pneumonectomy (RV/TLC_{bp}) and at the follow-up (RV/TLC_{fu})

The Residual Volume.—

An alteration of the RV/TLC ratio can be due to a change in the RV, a change of the VC, or an alteration of both volumes mentioned, because

$$RV/TLC = \frac{RV}{RV + VC}.$$

In order to get an impression of the changes occurring after pneumonectomy, the RV/TLC_{fu} ratio for each patient is compared with the RV/TLC_{bp} and the RV/TLC_{ad} ratio; the RV_{fu} with the RV

1. In Fig. 3, the RV/TLC_{bp} ratio is plotted against the RV/TLC_{fu} ratio for 63 patients; in 27 patients no RV/TLC_{bp} ratio was available. From the distribution of the points, the following conclusions can be derived: (a) in 92 per cent of the cases, the RV/TLC_{fu} ratio is greater than the RV/TLC_{bp} ratio, and (b) before the pneumonectomy, the difference between the mean RV/TLC ratios of both groups is statistically significant ($p = 0.01$). The same holds true for the mean ratios at the follow-up ($p = 0.04$). The change of the mean RV/TLC ratio caused by the resection is in both groups of the same proportion and proved to be statistically significant (Group I, $p = 0.01$; Group II, $p = 0.03$). The mean values are given in Table VII.

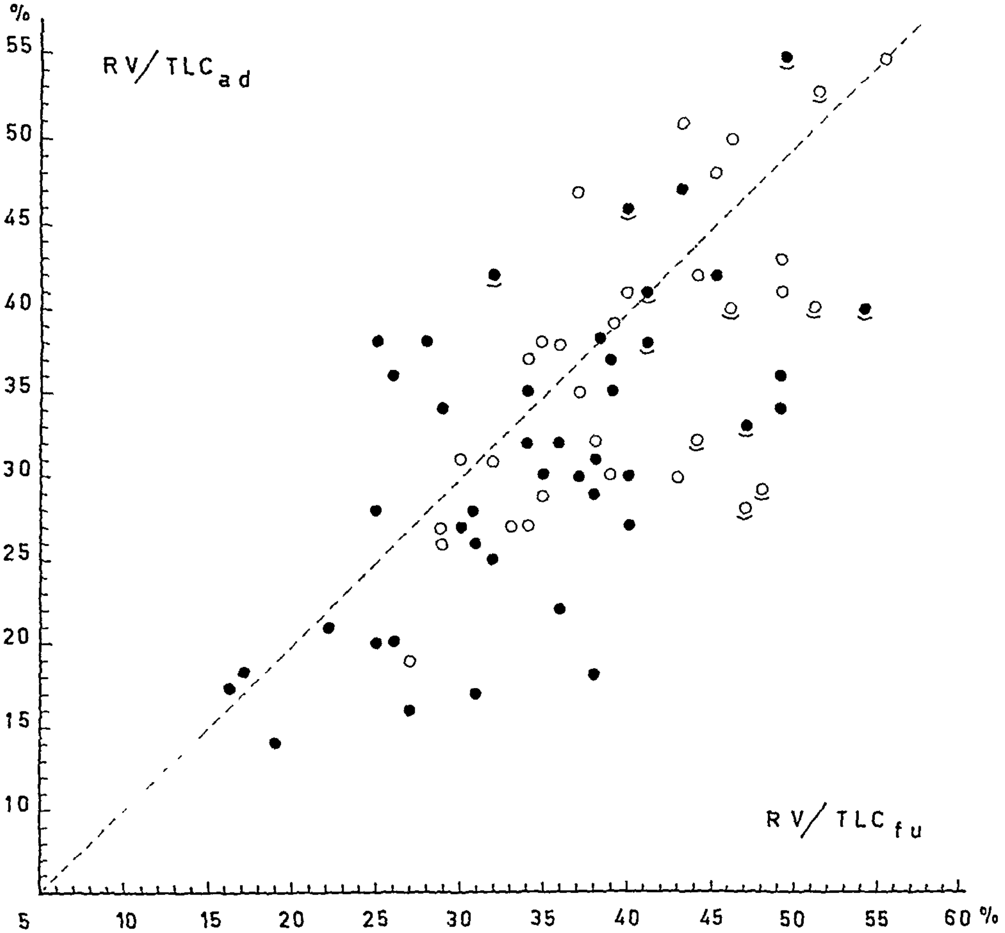

Fig. 4.—Comparison of the RV as a percentage of the TLC at the time of discharge from the sanatorium (RV/TLC_{ad}) and at the follow-up (RV/TLC_{fu}).

2. The change of the RV/TLC ratio in the period between the discharge from the hospital and the follow-up examination is given in Fig. 4. The distribution of the points in this figure shows an increase of the RV/TLC ratio in 65 per cent of the cases, equally distributed over the two groups. From this it is concluded that the difference between the RV/TLC ratios for Groups I and II did not change significantly following discharge from the hospital ($p = 0.3$).

3 Since the increase of the RV/TLC ratio can be due both to an increase of the RV and to a decrease of the VC, it is necessary to study the changes of the absolute RV values In Fig 5, the changes of the absolute values of the RV, before and after pneumonectomy, are given In 70 per cent of the cases, equally distributed over the two groups, an increase of the RV was found Consequently, the increase of the RV/TLC ratio after pneumonectomy was, for the greater part of the cases, not only due to a decrease of the vital capacity (Fig 1) but also to an increase of the residual volume

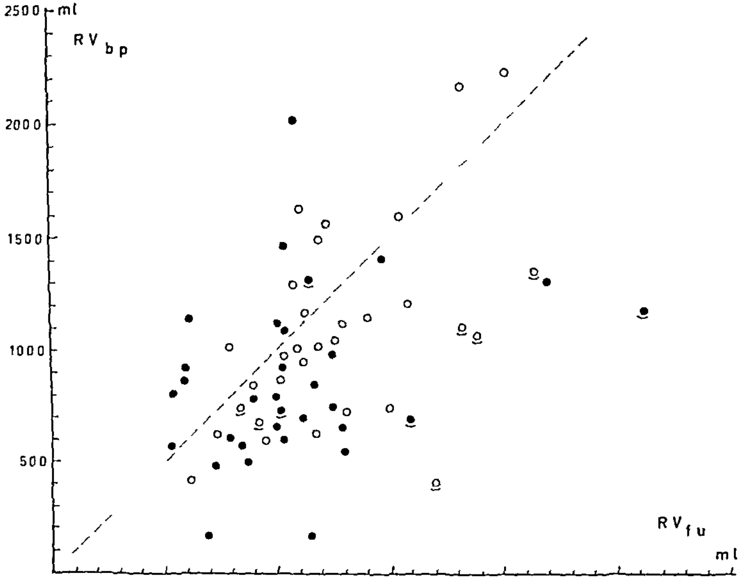

Fig 5.—Comparison of the RV in milliliters before the pneumonectomy (RV_{bp}) and at the follow up (RV_{fu})

4 The increasing age of the patients must be taken into account in judging the change of the RV/TLC ratio in the postoperative period The average interval between the discharge from the sanatorium and the follow-up examination amounts to 41 months Within this period, the mean RV/TLC ratio of Group I changed from 31 to 34 per cent and that of Group II from 37 to 40 per cent It is improbable that these differences can be explained by the slight increase in age

Reviewing these data, the conclusion can be drawn that in both groups the increase of the RV/TLC ratio during the first 11 months after the pneumonectomy (Period bp/ad) is mainly due to a decrease of the VC, while the RV is relatively constant In the period of about 41 months after the d[illegible]ge [illegible]iod ad/fu), the increase of the RV/TLC ratio is due to an increase of the RV, while the VC is almost constant. This phenomenon is graphically demonstrated in Fig. 6.

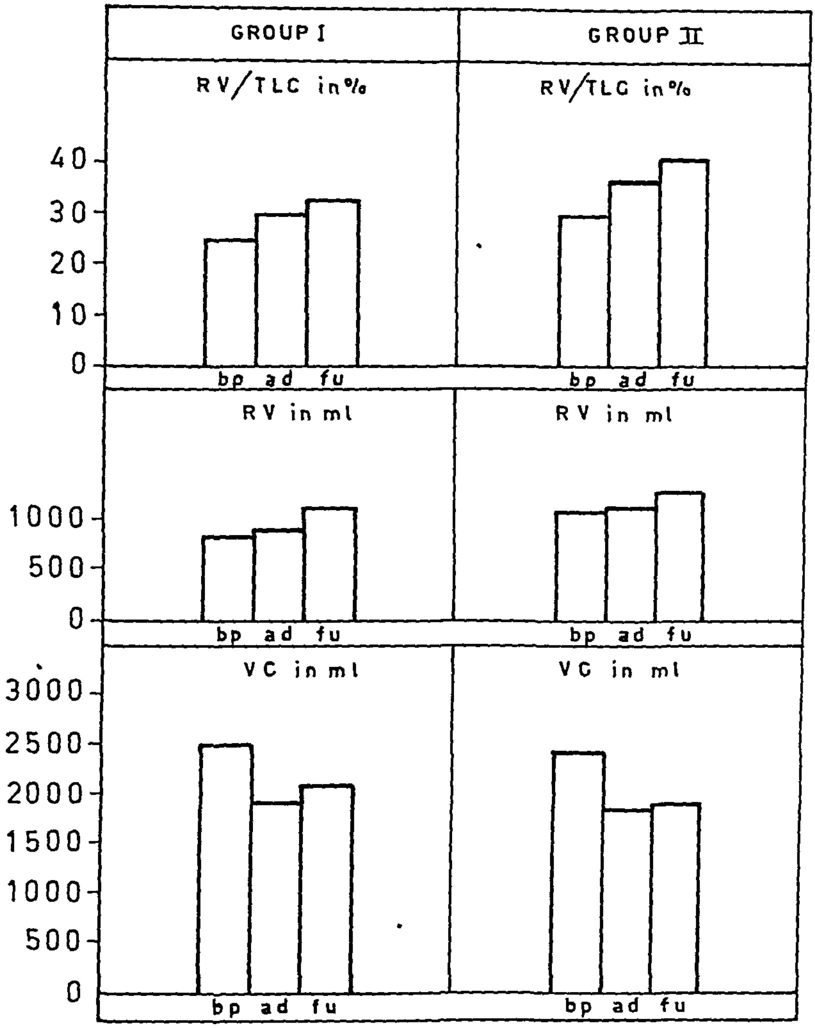

Fig. 6.—Comparison of the VC in milliliters, RV in milliliter and the RV/TLC ratio, before pneumonectomy (bp), at discharge (ad), and at follow-up (fu).

The Functional Residual Capacity.—

The FRC at rest and during hyperventilation, before the pneumonectomy and at the follow-up examination, is related to the ERV (FRC - RV) and to the shift of the expiratory level during maximal hyperventilation (Table VI). Some remarkable differences between the patients without (Group I) and with a thoracoplasty (Group II) were found: (a) In Group I the RV increased significantly ($p = 0.04$) in the period bp/fu, while the ERV was constant. In Group II, on the contrary, the significant increase of the RV ($p = 0.04$) was coupled with a comparable significant decrease of the ERV ($p = 0.02$). (b) During hyperventilation, MBC, hardly a rise of the expiratory level occurred in Group I, while before the pneumonectomy this shift was highly significant ($p = 0.005$). In Group II, the shift of the expiratory level was evident both before and after the pneumonectomy.

TABLE VI. THE SUBDIVISIONS OF THE FRC AT REST (FRC^r) AND DURING HYPERVENTILATION (FRC^h) IN MILLILITERS

	POINT OF TIME	RV	ERV	FRC^r	FRC^h	SHIFT OF THE EXPIRATORY LEVEL
Group I	bp	860	490	1,350	1,660	+ 310
	fu	1,050	510	1,560	1,620	+ 60
Group II	bp	1,070	530	1,600	1,980	+ 380
	fu	1,280	340	1,620	1,960	+ 340
Total	bp	950	520	1,470	1,840	+ 370
	fu	1,110	390	1,500	1,680	+ 180

The Timed Vital Capacity.—

Generally, the TVC is expressed in relation to the VC—TVC/VC ratio. In our material it became evident that, in both groups of patients, the ratios before the pneumonectomy and those at the follow-up were equal (Table VII)—the TVC decreased in the same measure as the VC. Moreover, it could be proved from the TVC curves that the maximum volume of gas, expired in every space of time within one second, was diminished in proportion to the alteration of the VC. The question arises, however, as to whether or not the constancy of the TVC/VC ratio means that the pulmonary function with regard to the TVC changed only quantitatively. When performing the TVC, the expiratory forces do not act upon a gas volume that equals the VC, but upon a volume equivalent with the TLC. Therefore, it seemed more reasonable to express the TVC in relation to the TLC (TVC/TLC ratio). By calculating the TVC/TLC ratio before the pneumonectomy and at the follow-up, a statistically significant difference between both values (Group I, $p = 0.04$; Group II, $p = 0.05$) could be shown (Table VII). The differences between the TVC/TLC ratios of both groups before the operation as well as at the follow-up study proved to be significant ($p_{bp} = 0.004$; $p_{fu} = 0.005$).

TABLE VII. THE MEAN VALUES OF THE RV/TLC, TVC/VC, AND THE TVC/TLC RATIOS AND THE MBC IN PATIENTS WITH AND WITHOUT A THORACOPLASTY IN ADDITION TO A PNEUMONECTOMY

	POINT OF TIME	RV/TLC	TVC/VC	TVC/TLC	MBC IN L./MIN.	
					ACTUAL	PREDICTED
Group I	bp	25	66	51	49	51
	fu	34	66	44	39	41
Group II	bp	30	60	42	44	44
	fu	40	61	37	34	36

The Maximum Breathing Capacity.—

In both Groups I and II, there was a significant decrease of the MBC in the period between the pneumonectomy and the follow-up (Group I, $p = 0.005$;

Group II, p = 0.003. The relation between the actual and the predicted value of the MBC was a very close one (r = 0.978; Sr = 0.100) (Table VII).

The Relation Between the TVC and the RV.—

In order to get an impression about the relation between the TVC/TLC and the RV/TLC ratios in the patients at the time of the follow-up, the correlation diagram for these data is constructed (Fig. 7). There is a definite negative correlation between the RV/TLC and the TVC/TLC ratio (r = -0.816; Sr = 0.036) and this correlation proved to be far better than that between the formerly used TVC/VC and the RV/TLC ratio (r = -0.456; Sr = 0.084) (Fig. 8). Since in Fig. 7 both the RV and the TVC are related to the TLC, a good correlation between the absolute values of the RV and TVC is present too. The amount of gas that maximally can be expired in the first second after a maximal inspiration is evidently correlated to the residual volume in patients without and with a thoracoplasty, in addition to a pneumonectomy. As could be expected, nearly all patients of the asthmatic group are localized in the left part of the diagram.

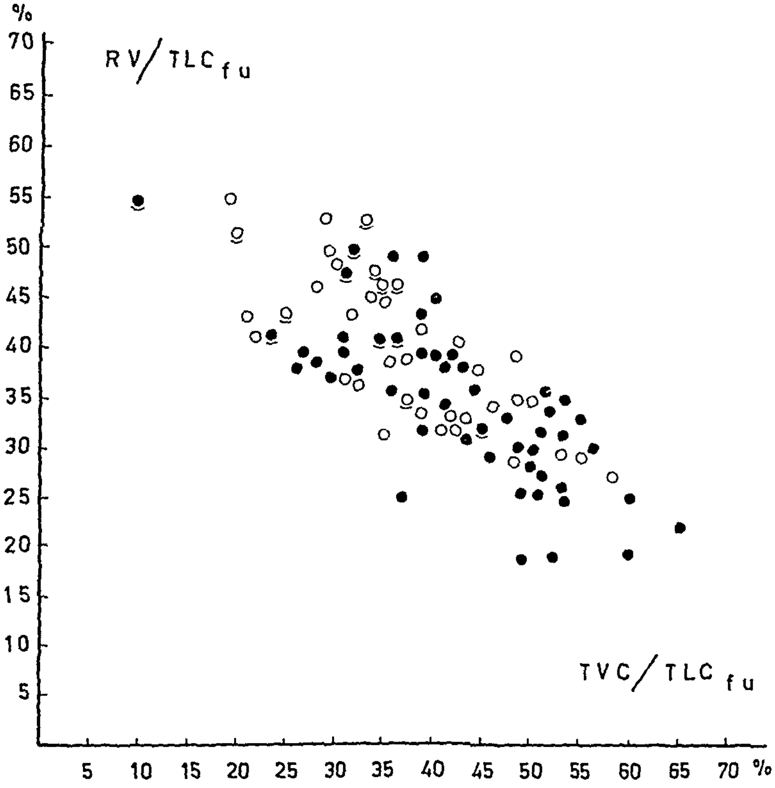

Fig. 7.—Relation between the RV/TLC ratio and the TVC/TLC ratio at the follow-up examination.

CONCLUSIONS AND DISCUSSION

By surveying the literature on pulmonary function in patients who underwent a pneumonectomy, it is evident that the character of the data published makes a comparison difficult for one or more of the following reasons: the time interval between pneumonectomy and follow-up is short, the data and conclusions concern small groups of patients, the data are incomplete or are only given as relative figures, the methods used differ in some extent, and the data concern nonhomogeneous groups as to the underlying diseases.

From the data reported in this paper the following conclusions can be drawn:

(a) As a result of the elimination of the vital capacity of the diseased lung by pneumonectomy, the VC_{fu} is significantly smaller than the VC_{bp} (Fig. 1). As for the whole material, no difference could be found between the VC of the contralateral lung before the operation and the VC at the follow-up

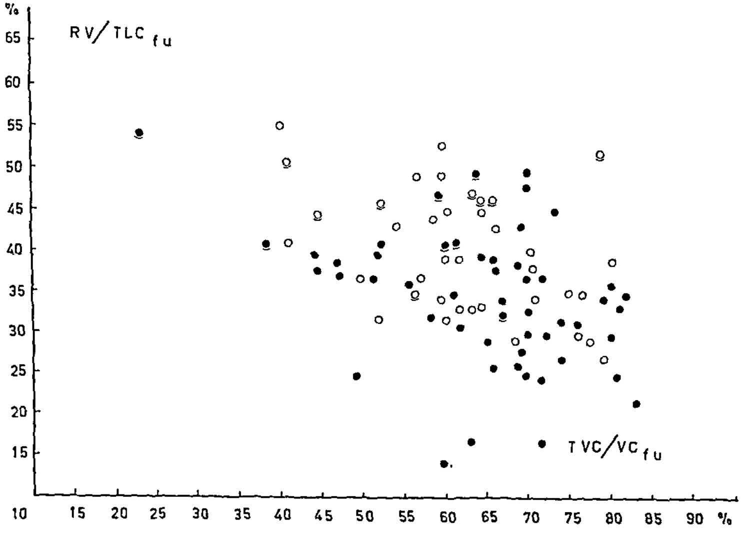

Fig. 8.—Relation between the RV/TLC ratio and the TVC/VC ratio at the follow-up examination.

study (Fig. 2). If, however, the material is divided into patients without (Group I) and with a thoracoplasty (Group II), a significant difference in this respect could be demonstrated between the two groups (Table IV). In Group I, the VC of the remaining lung was slightly increased in the period bp/fu; in Group II, on the contrary, the VC of the contralateral lung was decreased in that period. This decrease proved to be due mainly to the data of the patients who underwent their thoracoplasty after the pneumonectomy. Therefore, it seemed likely that thoracoplasties have an unfavorable influence on the vital capacity of the remaining lung. From the data of Table V, it is evident that the condition of the contralateral lung before the pneumonectomy and the adaptability of this lung after the operation also accounts for a difference between the VC_{br} and the VC_{fu}. An increase of the VC of the remaining lung after the operation was found only when the participation of the resected lung in the total pulmonary function was relatively great (27 to 45 per cent). If, on the contrary, the function of the diseased lung was small (15 to 26 per cent), the remaining lung was apparently already partly adapted to the pathologic intrathoracic conditions before the operation and no change of the VC of that lung occurred. In the group wherein the participation of the resected lung in the VC ranged from 0 to 14 per cent, the difference between the expected loss and the actual loss was partly due to the influence of the thoracoplasty.

(b) The absolute values of the residual volume before the pneumonectomy and at the discharge from the hospital are about the same (Fig. 6). From this and from the fact that the RV of the diseased lung is eliminated by pneumonectomy it is evident that the RV of the remaining lung has increased after the operation; this holds true for both groups. The extent of the increase of the RV of the remaining lung could not be measured, because the unilateral determination of the RV was not yet at our disposal at that time. In the period between the discharge and the follow-up studies, an increase in the RV of the remaining lung was found, both in patients with and without a thoracoplasty (Fig. 6). So, in our material, an increase of the RV could not be prevented by a thoracoplasty.

(c) The TLC of the remaining lung in the postoperative period is gradually increased and this increase is for the greater part due to the change of the residual volume (Fig. 6). If the increase of the TLC is a measure of the distention of the remaining lung tissue, the distention was in most of the cases not serious and was not prevented by thoracoplasty.

(d) Many investigators have shown that, after pneumonectomy, the RV/TLC ratio, compared with the normal calculated ratio, was increased.[2, 4, 5, 6, 8, 13] Hirdes and Bosch,[9] on the other hand, found that in patients who underwent a pneumonectomy without a thoracoplasty, a decrease of the RV/TLC ratio occurred. From their data, it can be calculated that the absolute value of the RV did not change but that the decrease of the RV/TLC ratio was only a relative one due to the increase of the VC. In our material, the increase of the RV/TLC ratio was due mainly to a decrease of the VC as a consequence of the resection and later on preponderantly to an increase of the RV of the remaining lung. This holds true whether thoracoplasty was performed or not. In our material, the change of the RV/TLC ratio cannot be explained by the aging of the patients. In Group II, the RV/TLC ratio was significantly greater than in Group I, both before and after the pneumonectomy (Table VII). It could not be proved, but it seemed likely, that this difference is caused preponderantly by the presence of the thoracoplasty.

(e) Although the RV/TLC ratios of both groups differed at the time of the follow-up study, the FRC^{r}/TLC_{fu} ratios were almost equal (Table VI).

This was due to a difference of the ERV_{fu} of both groups During hyperventilation, on the contrary, the FRC^h/TLC_{fu} ratio of Group II differed significantly from the FRC^h/TLC_{fu} of Group I These findings suggest that, in rest, the efficiency of the ventilation in both groups was almost equal while, during hyperventilation, the ventilation of the patients with a thoracoplasty was less efficient

(f) Most of the authors found the TVC/VC ratio unchanged after pneumonectomy That means that the TVC changed in the same proportion as the VC In our two groups, the TVC/VC ratios were identical before the operation and at the follow up study For judging the expiratory capacity, however, the TVC/TLC ratio proved to be a far better criterion than the TVC/VC ratio, because the changes of the RV are now taken into account In both groups of patients, a significant difference between the TVC/TLC_{bp} and TVC/TLC_{fu} ratios was present This difference points to the fact that a qualitative loss of the pulmonary function really occurred in both groups Moreover, it could be proved that the expiratory capacity of patients with a thoracoplasty was significantly worse than that of the patients without a thoracoplasty

(g) Van Veen and Hindes[19] found a rather good negative correlation between the TVC/VC and the RV/TLC ratio in a large number of patients without asthmatic symptoms in several lung diseases In our material, an evident negative correlation between the TVC/TLC and the RV/TLC ratio was demonstrable, even when patients with asthmatic symptoms were included

From the data of this paper, it is concluded that thoracoplasty neither prevented distention nor increased the efficiency of ventilation or the expiratory capacity This is in agreement with the findings of Gaensler and Strieder[7]

Whether, at the time of the follow up study, the remaining lung was in a stabilized condition or if, in addition to the aging process, progressive changes were taking place could not be established In order to gain any further insight into the fate of the remaining lung, it is of utmost importance to make repeated examinations of the pulmonary function at regular intervals

The conclusions drawn in this paper are based on the functional data of a relative nonhomogeneous group of patients Although the results are based on the data of a relative large number of patients the reliability of the conclusions is only relative, because it is extremely difficult to take into account all factors influencing pulmonary function

SUMMARY

1 The results of the pulmonary function tests in 90 patients who underwent pneumonectomy for pulmonary tuberculosis are presented The data at the time of the follow-up study (average of 52 months after the operation) are compared with those obtained before the pneumonectomy and with the data of the pulmonary function 11 months after the operation The patients are

divided into two groups: those without a thoracoplasty (Group I) and those who underwent a thoracoplasty before, during, or after the pneumonectomy (Group II).

2. The *vital capacity* showed a significant decrease after pneumonectomy, which corresponded well with the expected loss, as could be calculated from the bronchospirometric data. The presence of a thoracoplasty, as well as the quantity of functioning lung tissue removed, influenced the VC of the remaining lung at the follow-up study.

3. The absolute value of the *residual volume* was not changed by the operation as judged by the early postoperative study. At the time of the late follow-up study, the RV had increased in both those with and without a thoracoplasty. In the period between the pneumonectomy and the discharge from the hospital, the increase of the RV/TLC ratio was due mainly to a decrease of the VC, whereas the RV was unchanged. In the period after the discharge, the further rise of the RV/TLC ratio occurred because of an increase of the RV in the face of a nearly stable VC. The enlargement of the RV/TLC ratio is not explainable by age changes alone.

4. The *functional residual capacity* at rest showed no significant difference in the two groups. This was not true for their subdivisions—RV and ERV. During maximal hyperventilation (MBC), the FRC showed a significant increase in Group II, while in Group I a rise of the expiratory level could hardly be demonstrated.

5. The *timed vital capacity* in relation to the VC (TVC/VC ratio) was unaffected by pneumonectomy. The TVC/TLC ratio proved to be a better criterion for judging the changes of the expiratory capacity than the TVC/VC ratio. The pneumonectomy caused a significant change in the TVC/TLC ratio in both groups of patients.

6. A clear negative correlation between the RV and the TVC could be demonstrated both in patients with and without a thoracoplasty.

7. The presence of a thoracoplasty in patients who underwent a pneumonectomy proved to have no preventive influence on the distention of the remaining lung tissue and affected the efficiency of the pulmonary function in an unfavorable way.

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THE PATTERNS AND DYNAMICS OF TRACHEOBRONCHIAL DEFORMITY IN PULMONARY TUBERCULOSIS

G. A. P. Hurley, F.R.C.S.(C), and D. Todosijczuk, M.D., Montreal, Quebec

MANY conditions of disease in which the process of healing results in deformity of structure with great impairment of function are well recognized. Such instances as the stenosed mitral valve after acute rheumatism, the obstructed duodenum after peptic ulcer, the grotesque appearance after facial burns, and the old rigid thick-walled tuberculous cavity resisting closure, come to mind. In these, what might be called "errors of healing," the process of scar replacement and the ever-present tendency of scar tissue to contract, are the governing factors. It is as if the healing process overshoots the mark, and instead of restoring the status quo ante, actually brings about new and important disability.

These errors of healing are well exemplified in disease of the hollow organs and passages of the body. In the case of the tracheobronchial passages, healing errors are extremely frequent, and result not only from intrinsic disease of the air passages themselves, but also from disease of the pulmonary parenchyma to which they provide access. They are particularly prevalent in pulmonary tuberculosis, a disease which, by reason of its long duration and great destructive power, causes the most serious deformities of the bronchopulmonary system.

It should be emphasized that much of this tracheobronchial deformation cannot be detected in the routine x-ray studies of the chest, and can only be exposed by bronchography. It is only in the past few years that bronchography has become freely used in pulmonary tuberculosis, because of real or imagined dangers due to the effects of the heavy iodized oils, and their undesirably prolonged staining of the chest roentgenogram. The advent of the water-soluble, rapid-clearing bronchographic media, such as dionosil, has made bronchography in pulmonary tuberculosis practical and safe. Indeed, it might be said that bronchography now should be just as important a part of case evaluation before surgery in pulmonary tuberculosis as it has so long been in bronchiectasis. With the modern precise resection techniques, a careful mapping of the bronchpulmonary system is essential so that diseased segments can be removed and healthy segments preserved.

From The Royal Edward Laurentian Hospital, Ste. Agathe des Monts., P. Q., and the Grace Dart Hospital, Montreal, P. Q.

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In recent years, almost every case of pulmonary tuberculosis coming for surgical conference from the Royal Edward Laurentian Hospital, Ste. Agathe, and the Grace Dart Hospital, Montreal, has been subjected to bronchography. Some four hundred of these bronchograms have been reviewed, and this essay is an attempt to classify, correlate and, to some extent, explain the patterns of deformity found.

It should be pointed out, to begin with, that secondary bronchietasis, although frequent, is not a constant sequel to pulmonary tuberculosis, even extensive pulmonary tuberculosis. Of the cases studied, bronchiectasis was found in approximately 50 per cent. With regard to extent of disease, 55 per cent of the whole group were in the moderately-advanced, and 35 per cent in the far-advanced group.

In general, deformities of the tracheobronchial passages may be classified as (1) enlargement or dilatation of the lumen (bronchiectasis), (2) reduction or obliteration of the lumen (stricture), (3) abnormal curvature, and (4) abnormal angulation.

TABLE I. FOUR-HUNDRED BRONCHOGRAMS

Duration of Pulmonary Tuberculosis			
1. Longer than 2 years		196	49%
2. Shorter than 2 years		204	51%
	Total	400	100%
Extent of Pulmonary Tuberculosis			
1. Minimal disease		39	9.75%
2. Moderately-advanced disease		220	55.00%
3. Far-advanced disease		141	35.25%
	Total	400	100.00%

TABLE II. RIGHT LUNG DISEASE

1. Bronchograms of the right lung	Normal	65	21.81%
	Abnormal	233	79.19%
		298	100.00%
2. Bronchiectasis and shrinkage of RUL		147	49.33% of total or 63.09% of abnormal
3. Bronchiectasis without shrinkage of RUL		4	1.71% of abnormal
4. Shrinkage without bronchiectasis of RUL		22	9.44% of abnormal
5. Upward deviation of RUL bronchus		27	11.59% of abnormal
6. Abnormal angulation of right main-stem bronchus		7	3.00% of abnormal
7. Cavity present at the time of bronchogram		14	6.00% of abnormal

Tracheobronchial alterations may occur in different combinations and degrees, varying from mild, limited, or localized types, to extensive, generalized deformity. For example, abnormal curvature of the trachea, convex *to the side of the lesion, with secondary bronchiectasis of a diseased* upper lobe is a very frequent combination (Fig. 1). Less frequently, stricture or obliteration of a lobar bronchus with atelectasis and/or bronchiectasis of the lobe is seen.

The most interesting and important alterations in pulmonary tuberculosis, however, are found as part of a general deformation of the tracheobronchial skeleton, due to marked upward tracti[illegible] of the hilar structures (Fig. 2).

It is well known that shrinkage of the diseased upper lung with elevation of the hilus is a common finding in pulmonary tuberculosis. Indeed, it has been generally regarded as a somewhat desirable thing, in that it implies or

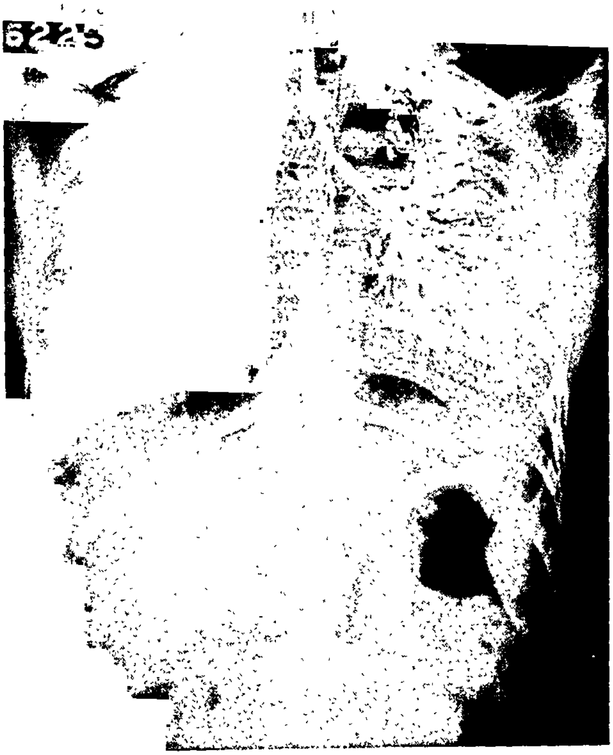

Fig. 1.

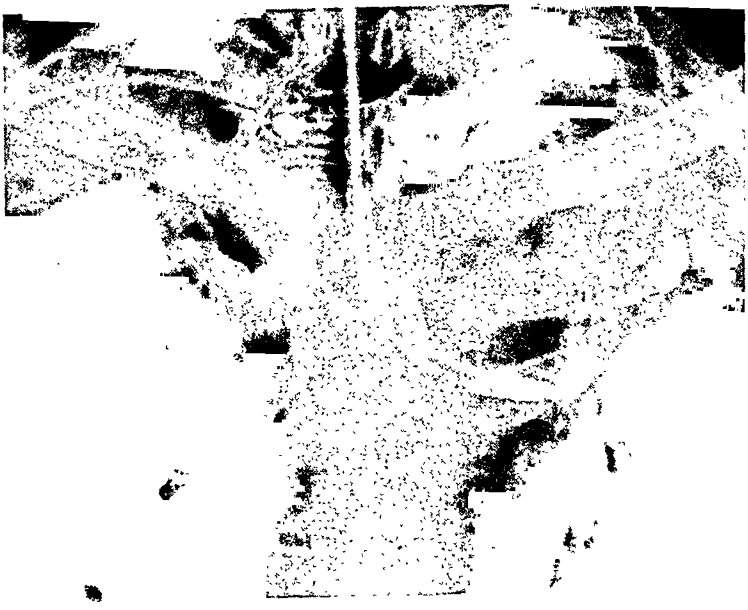

Fig. 2.

TABLE III. LEFT LUNG DISEASE

1. Bronchograms of the left lung	Normal	61	25.20%
	Abnormal	181	74.80%
	Total	242	100.00%
2. Bronchiectasis and shrinkage of LUL		131	54.13% of total or 72.38% of abnormal
3. Bronchiectasis without shrinkage		1	
4. Shrinkage without bronchiectasis		0	
5. Abnormal curvature of the left main-stem bronchus and abnormal angulation, junction left main-stem bronchus and left lower lobe bronchus		81	61.83% of diseased LUL; 44.75% of abnormal
6. Cavity present at time of bronchogram		19	10.05% of abnormal

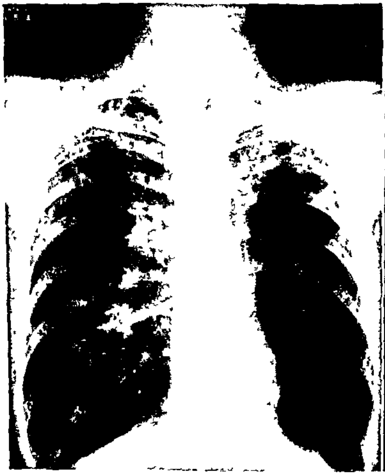

Fig 3

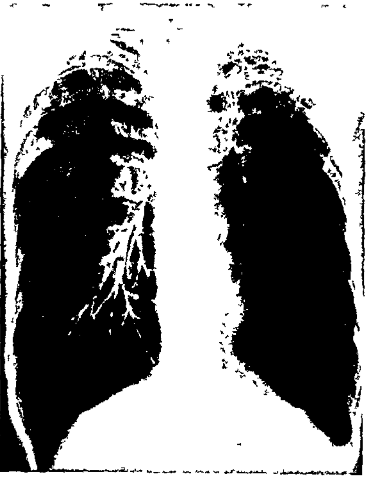

Fig 4.

is thought to imply sound fibrous healing of the lesion. Not enough attention has been paid, however, to the deleterious effect on function of this upward pull on the hilus. This is no mere local shrinkage of organs, but a serious structural change of the bronchopulmonary alignment on the side in question or, in the case of bilateral disease, of the whole bronchopulmonary framework. So serious can this be that the ultimate result of an original lesion of the upper one third of the left lung, for example, may be virtually complete functional loss of the entire left lung, the upper lung being destroyed by tuberculosis and bronchiectasis, and the lower lung by emphysema (Figs. 3 and 4).

Such a condition is exemplified in Fig. 3. The bronchogram shown in Fig. 4, of the same case, illustrates the typical deformity resulting from upward traction displacement of the left hilus. The abnormal curvature of the left main-stem bronchus with pooling of the radiopaque liquid, and the abnormal angulation at the junction of the left main-stem and left lower lobe bronchus are the important features.

Due to anatomic differences as between the right and left sides, the effect of upward traction displacement is not as serious on the right as on the left, because the lower lung on the right is not so vulnerable.

This is explained by reference to certain differences in the anatomy of the bronchopulmonary system as between the right and left sides (Figs. 5 and 6). The left main-stem bronchus is much longer and it lies much more horizontally than the right main stem. Furthermore, it passes immediately beneath the arch of the aorta. If one regards both main stems as the arms of a lever (Fig. 5) with the fulcrum at the carina, it is clear that a relatively slight upward pull on the long left arm will have an equal effect to a much stronger pull on the short right arm.

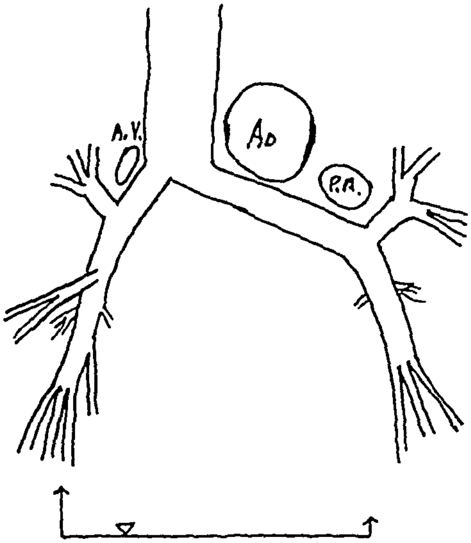

Fig. 5.

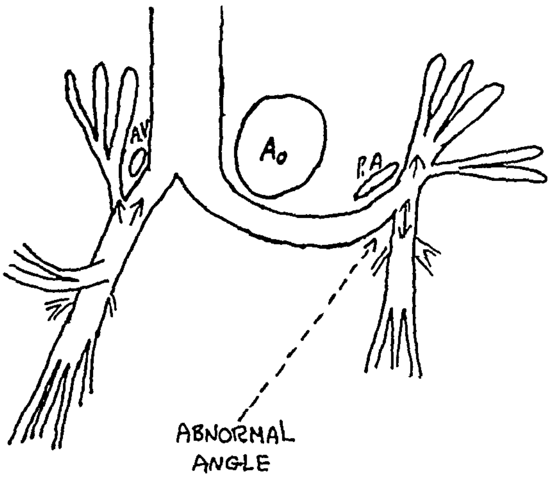

Fig. 6.

Hence, to begin with, upward traction displacement of the hilus is always more pronounced, and thus more serious on the left side. Normally, there is a gentle curving of the medial wall of the left main stem as it runs into the left lower lobe bronchus. When the left hilus is pulled up, the long left main stem winds itself around the arch of the aorta, into an abnormal curve, concave upward, and what was originally a gentle curve at the junction of the left main-stem and the left lower lobe bronchus now becomes an abnormal angle, which in long-standing cases may be as acute as 50 degrees. In the group under review, this angle varied between 50 and 130 degrees. This abnormal angulation obviously changes greatly the luminal axis of the left bronchial tree, and has a pronounced disturbing effect on its function.

In addition to the bronchus, all the structures of the hilus are involved in this change. The left pulmonary artery normally lies at first in front of the left main-stem bronchus, then winds up over the main stem before this branches into the upper and lower lobe bronchi. The artery then hooks around, as it were, behind the upper lobe bronchial arborization to emerge underneath it, and finally comes to lie in front of the lower lobe bronchus. When the left upper lobe arborization is pulled up, the artery is sharply kinked at the point where it crosses above the main stem and reduction in lumen with reduced blood flow to the left lower lobe occurs. Fig. 7 is a demonstration at autopsy of such an occurrence. Note the marked reduction in caliber of the pulmonary artery to the left lower lobe.

On the right side, a different picture presents itself. Here, because of the short, relatively vertical main stem, the upward displacement is practically confined to the more horizontal right upper lobe bronchus, which becomes more or less sharply angulated upward to lie more in the axis of the trachea. This is usually accompanied by bronchiectasis of the right upper lobe. A further stage of the deformity, and a typical occurrence on the right side, is obliteration of the lumen of the right upper lobe bronchus, the right upper lobe itself coming to lie, a shrunken atelectatic remnant, against the mediastinum (Fig. 8). This is reminiscent of the well-known middle lobe syndrome.

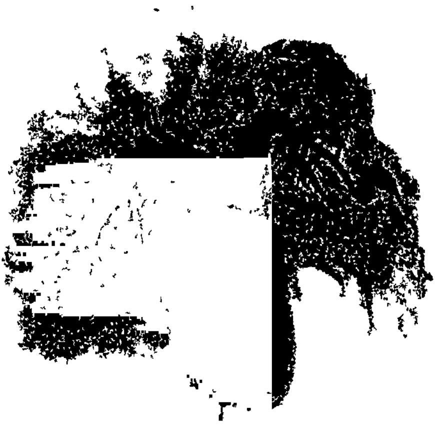

Fig. 7.

In a few instances of long-standing disease with great shrinkage of the right upper lobe, we have found a slight degree of upward displacement of the right main stem, but this is unusual and never to the same extent as on the left side. Furthermore, there is no tendency toward curvature on the right because the small compressible azygos vein does not offer the same resistance as the large thick-walled aorta on the left.

It should be noted here, therefore, that the ultimate effect of upward traction displacement on the right side is exerted on the right upper lobar hilus, while on the left side it is exerted on the entire pulmonary hilus. This may explain the greater vulnerability of the left lung and the fact that the right lower and middle lobes are not so liable to become emphysematous.

The effects of these changes in lumen and alignment are, we believe, responsible for profound disturbances of function. The first and perhaps the most obvious effect is fixation or relative fixation of the hilar area by this strong upward pull, acting as a taut guy rope on the hilar bronchial branching. Thus, the normal up and down movement of the hilus on expiration and inspiration, respectively, is greatly hindered or prevented. This is apt to restrict ventilation to a marked degree, since it acts in direct opposition to the normal downward pull of the diaphragm. In this way, it hinders the easy downward expansion of the parenchyma, as the bronchial tree moves downward and to some extent inward on inspiration.

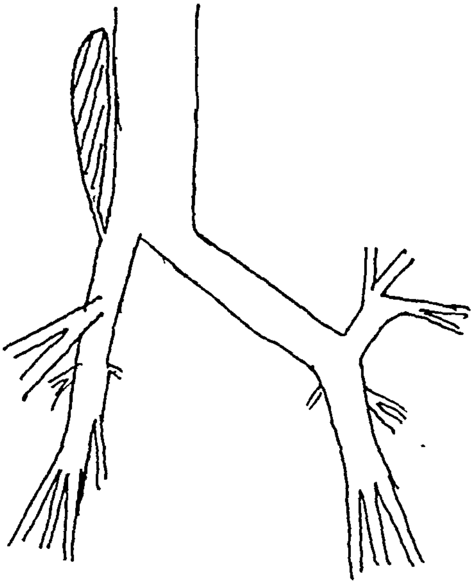

Fig. 8.

Another obvious effect is impaired gas exchange, due to reduction in lumen of the left pulmonary artery, and hence lessened blood supply, particularly to the left lower lobe. Incidentally, some observers believe that emphysema can develop as a direct result of reduced pulmonary artery blood flow. The effects of stimulation due to traction on the elements of the hilar nerve plexus could be significant, but the importance of this can only be guessed at.

Probably the most far-reaching effects, however, are due to the altered caliber and alignment of the air passages with resulting changes in the dynamics of bronchopulmonary air flow. Currents of gas like rays of light tend to travel in straight lines. When a current of air comes up against an obstruction or partial obstruction in a bronchial passage, such as a stricture or a sharp angulation, or a pronounced curve, there is hindrance to air flow. The result of this is deflection of the stream, secondary currents and eddies, and perhaps most important, reverse currents of flow. In quiet respiration this may not interfere too much with function. In deep forcible breathing, however, there may be considerable disturbance and this is first and chiefly felt in interference with air exit. In a markedly impaired lumen, there is also interference with air entry, but the first disturbance is difficulty in emptying rather than filling the lungs. The normal dilatation of the bronchial passages on inspiration, and their corresponding contraction on expiration accentuates the obstructive effect of abnormal angulation or stricture, particularly with respect to air exit. The ultimate effect is the phenomenon known as "air trapping."

The most extreme conditions of air flow occur in cough, and particularly in forcible, violent, prolonged and repeated cough, and under these conditions the most intense disturbance of bronchopulmonary dynamics is apt to occur. Reverse currents of air flow, now become reverse shock waves, and instead of simple air trapping, there occurs a powerful abnormal backward thrust on the walls of the distal bronchi and alveoli.

Rahn has estimated that in a particular phase of cough the air is traveling at speeds in the realm of 200 to 300 miles per hour. Beck has reported air flow rates of 12 L. per second at the mouth, at the moment of glottic opening in cough, and says that the air speeds reached here are sometimes higher than the speed of sound, namely, 732 miles per hour. Beck also reports that during the glottic closure phase of cough, the intrathoracic pressure in normal subjects ranges between 80 and 110 mm. Hg, while in patients with bronchopulmonary disease, the pressure may be increased over 120 mm. Hg. We have measured the intrabronchial pressures during cough, and in forcible cough have registered pressures as high as 180 mm. Hg in the lower lobe bronchi. These figures give an idea of the magnitude of the forces that are operative in the bronchopulmonary system during cough. It is understandable, therefore, that a possible result of the long-continued action of these forces may be collapse or blow out of the walls of bronchi or alveoli, encouraging or causing, in the one case, bronchiectasis and, in the other, emphysema. The association of emphysema with the cough-producing propensities of chronic bronchitis, and of bronchiectasis with a history of whooping cough in childhood is, perhaps, significant.

Not enough emphasis, we believe, has been placed on violent uncontrolled cough as an injurious factor leading to extensive lung destruction. In patients with lung disease, cough is apt to be more prevalent and forcible in order to get rid of abnormal secretions or because of mucosal irritation. Again, if the bronchial passage is deformed, it becomes more difficult to move secretions through it. Moreover, people differ widely with respect to the control which they exercise over the function of cough. Coughing, like scratching, is a physiologic mechanism designed to remove an irritant to a body surface. It is always available, but is intended to be used only when needed, and then nicely graded to the extent of the need. One cough, like one scratch, borrows another, and uncontrolled coughing or scratching can result in serious damage to the structures acted upon.

Let us again consider (see Figs. 5 and 6) the altered structure of the bronchopulmonary skeleton in upward traction displacement of the hilus, and the effect of these alterations on function. Normally the expired air coming up from the lower lobe flows easily into the left main-stem bronchus and thence into the trachea. When the left hilus is pulled up, however, the air current from the left lower lobe will tend to flow into the dead end of the diseased upper lobe because the left upper lobe bronchus is now in more or less direct line with the left lower lobe bronchus, whereas the left main stem has actually taken a turn in the opposite direction. This obviously impedes the exit of air from the left lower lobe. In cough, there is added a powerful abnormal backward thrust on the alveolar walls of the left lower lobe, and a forward thrust on the already diseased and weakened bronchi of the left upper lobe.

In upward traction displacement of the right hilus, there is a similar though less marked abnormal forward thrust on the diseased bronchi of the right upper lobe, but there is obviously never the same degree of obstruction to air exit and hence not the same degree of abnormal backward thrust on the alveolar walls of the right lower lobe.

It is difficult, except in advanced cases, to detect the presence of emphysema on the chest roentgenogram, but we have had occasion to remark on the relative frequency of emphysema of the left lower lobe in pulmonary tuberculosis.

The finding in chronic phthisis of upper lobe shrinkage with lower lobe emphysema is common. The emphysema is usually designated as compensatory. It is assumed that the uninvolved lower lung dilates to fill the space vacated by the shrunken diseased upper lung. If it were merely a need to fill space, however, one would expect the diaphragm to move upward in order to reduce the need, as it usually does after lobectomy on the side in question. Furthermore, one would expect not the lower lung but the mid-lung to dilate since this is the part contiguous to the diseased portion and hence should be the part first and chiefly subjected to this presumed upward call for space-filling tissue. Neither of these things happen, however. In fact, the diaphragm moves downward instead of upward, and the part of the lung that becomes emphysematous is the lower and not the mid-zone. This suggests that the so-called compensatory emphysema is the result of a different and possibly much more complex mechanism than the one usually supposed. It is highly possible that the emphysema is obstructive rather than compensatory, and it could develop as the result of upward traction displacement of the hilar structures and poorly controlled cough.

In the course of this study we found it convenient to recognize a left lung syndrome, and a right upper lobe syndrome (Tables IV and V).

TABLE IV. LEFT LUNG SYNDROME

1. Upward traction displacement of left hilus
2. Abnormal curvature left main-stem bronchus
3. Abnormal angulation at junction of left main-stem bronchus and lower left lobe bronchus
4. Bronchiectasis, left upper lobe
5. Emphysema, left lower lobe (final stage)

TABLE V. RIGHT UPPER LOBE SYNDROME

Stage 1
1. Abnormal angulation or partial occlusion right upper lobe bronchus
2. Bronchiectasis, right upper lobe.

Stage 2
1. Marked abnormal angulation and complete or almost complete occlusion right upper lobe bronchus
2. Atelectasis, right upper lobe

SUMMARY

We believe the most significant finding of this study is the evidence pointing to the undesirable effects of upward displacement of the hilus, particularly on the left side, in chronic pulmonary tuberculosis This points up the need for vigilance, especially in tuberculosis of the left upper lobe, to anticipate and if possible prevent the destructive effects of this displacement.

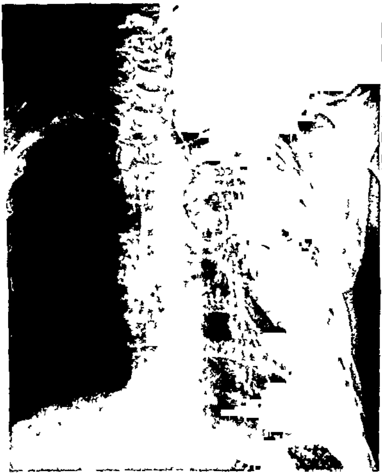

Fig 9

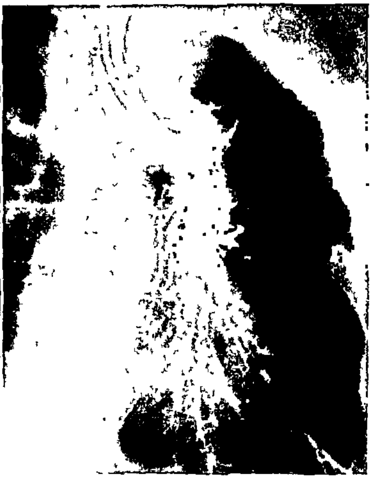

Fig 10

What are the chances for preventing or interrupting such a development?

Prevention is obviously best served by prompt treatment of the tuberculosis in order to diminish the amount of contracting scar tissue. We suspect also that the reduction or elimination of useless forcible cough is important.

In order to interrupt the deforming process, it would seem as if the only logical way of proceeding would be to remove the contracting mass of fibrous tissue in the left upper lung as soon as it is observed to be causing abnormal curvature of the left main-stem bronchus, and abnormal angulation at the junction of the left main stem and left lower lobe bronchi. This would be a new indication for removing an area of disease, even apparently healed disease in the left upper lung. In cases in which, for some reason, resection of the left upper lung is not practical, an alternative might be found in upper thoracoplasty with apicolysis, pushing the contracting mass down to the level of the hilus where its upward pull is neutralized.

When deformity is already far advanced and the left lung syndrome well established, there is less hope for useful remedial measures. However (Figs. 9 and 10) in some cases of this kind, resection of the left upper lobe with upper thoracoplasty does seem to correct, at least in part, the abnormal curvatures and angulation, and in this way tend to interrupt the harmful series of events leading to loss of function of the left lower lobe.

The authors wish to acknowledge the kind cooperation of the Medical Director and staffs of the Royal Edward Laurentian Hospital and the Grace Dart Hospital.

THE SURGICAL TREATMENT OF AORTIC INSUFFICIENCY BY CONVERSION OF THE TRICUSPID AORTIC VALVE TO A BICUSPID VALVE

Chronic Experimental Studies

Joseph J Garamella, M D , Ph D , James G Andersen, M D , Reuben Oropeza, M D , Angelo Veloso, M D , and R Naidu, M D ,*
Minneapolis, Minn

IN PREVIOUS communications,[1, 2] a method of aortic valvuloplasty was described for the surgical treatment of aortic insufficiency The method consists of total excision of the noncoronary aortic cusp with a corresponding triangular segment of the base of the aorta (Fig 1) By suture repair, the normal

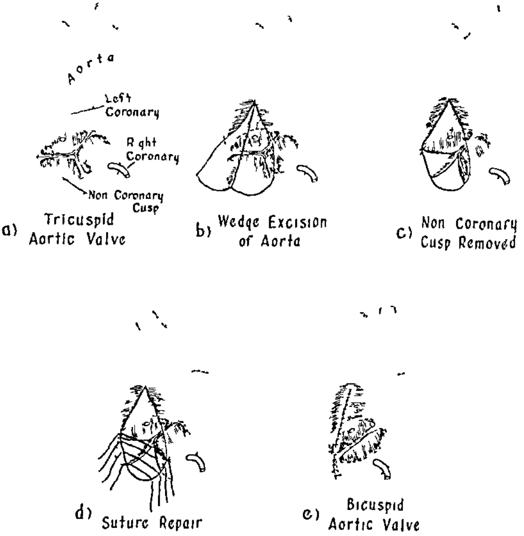

Fig 1 —Conversion of tricuspid aortic valve to bicuspid valve

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From the Jay Phillips Laboratory Mount Sinai Hospital Minneapolis Minn and Department of Surgery University of Minnesota Minneapolis

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*Present address 1029 Medical Arts Bldg Minneapolis Minn

Fig. 2.

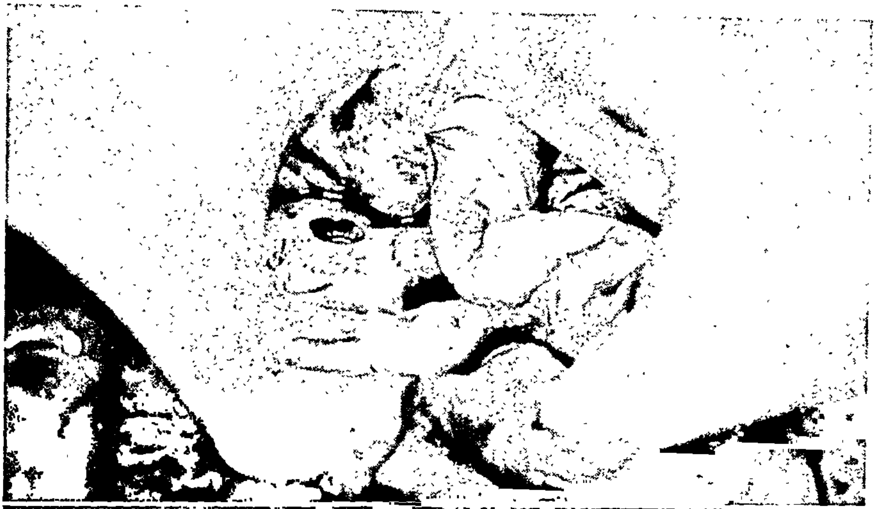

Fig. 3.

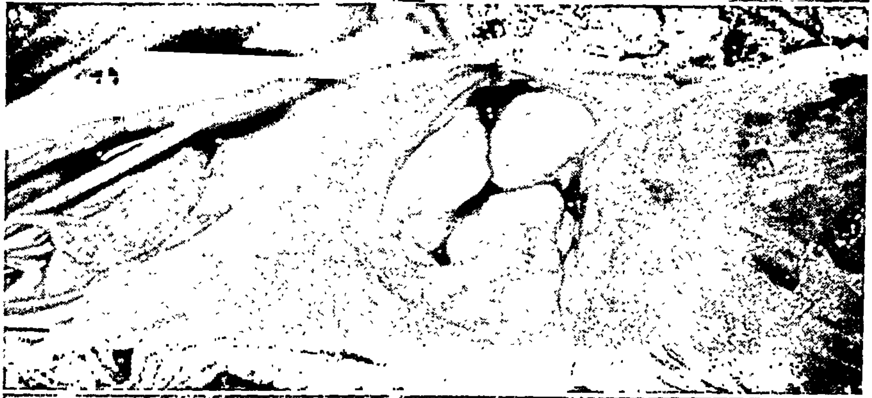

Fig. 4.

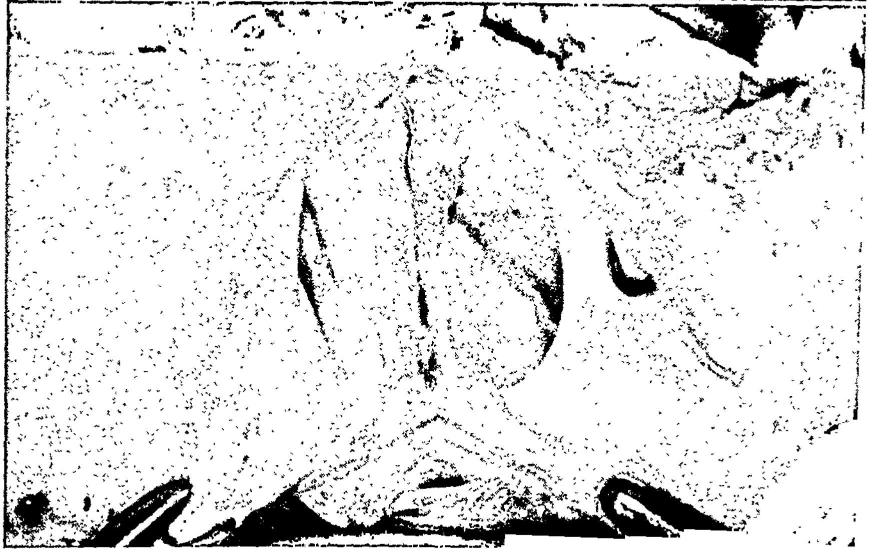

Fig. 2.—An autopsy specimen from a patient dying of aortic regurgitation shows the insufficient aortic valve viewed from above and posteriorly. Note the distortion, thickening, and shortening of the aortic cusps. The central defect causing aortic regurgitation is evident. The loss of cusp substance precludes complete coaptation. Dilatation of the aortic ring is not a conspicuous feature of this specimen.

Fig. 3.—Insufficient aortic valve viewed from below, the ventricular side, showing the central defect causing regurgitation. A partial rim of calcification is noted.

Fig. 4.—The incompetent aortic valve seen in Figs. 4 and 5 is viewed from above following plastic revision with total excision of the noncoronary aortic cusp. The valve is now bicuspid. The circumference has been reduced by one third. The two remaining coronary cusps appear to coapt well. The left coronary ostium is visualized to the left.

tricuspid aortic valve is converted to a bicuspid valve and the aortic circumference is reduced by one third. In effect, a severe degree of aortic insufficiency is produced and then surgically corrected by the valvuloplasty. Operative procedures were performed under direct vision with cardiac bypass employing an extracorporeal pump-oxygenator and elective cardiac arrest.

Short-term animal survival studies were described as well as functional evaluation in terms of pre- and postoperative arterial pulse patterns, transventricular and systemic pressure determinations, and retrograde aortography.

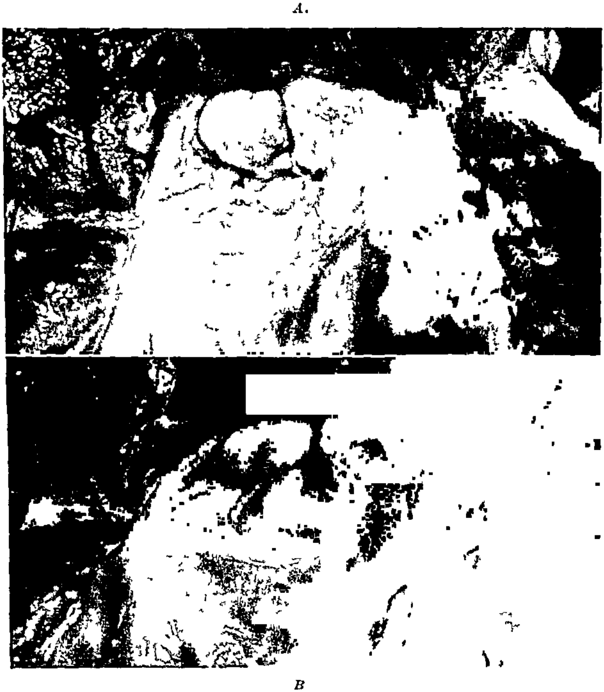

Fig 5—*A*, The incompetent aortic valve seen in Figs 4 and 5 is viewed from below, ventricular side following plastic revision The noncoronary aortic cusp has been excised The newly formed bicuspid valve appears to coapt well. Sutures in the line of repair are evident.

B, The aortic valve again viewed from the ventricular side The noncoronary aortic cusp remains in situ while the aortic wall has been reduced by one third The resultant coaptation appears less effective than in *A*, the noncoronary cusp seemingly herniating below the coronary cusps

Phases of systole were measured. No significant degrees of aortic stenosis nor aortic insufficiency were found in surviving animals Pathologic studies as evidenced in Figs 2, 3, 4, 5*A*, 6 support the clinical application of the principle.

Accordingly, it was felt that functional studies in chronic survival animals would be of interest and valuable and these form the basis of this report.

MATERIALS AND METHODS

Eleven chronic survivors with surgically produced bicuspid aortic valves were studied 26 to 405 days postoperative. The animals were anesthetized with intravenous Surital (thiamylal sodium), 75-100 mg. A No. 18 gauge needle was inserted percutaneously into the femoral artery. A No. 13 to 15 gauge

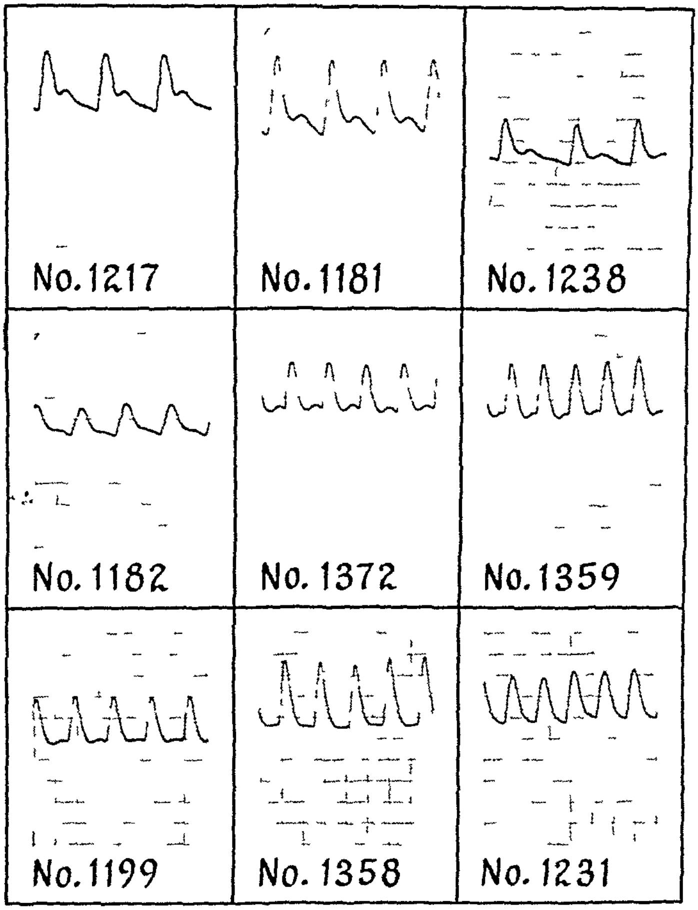

Fig 6 —Conversion of tricuspid aortic valve to bicuspid valve. Analysis of femoral pulse contours Chronic studies 26-317 days postoperative

TABLE I. CONVERSION OF TRICUSPID AORTIC VALVE TO BICUSPID VALVE CHRONIC STUDIES 26-317 DAYS POSTOPERATIVE

ANIMAL NO.	DAYS POSTOP.	DICROTIC FEMORAL CURVE	B.P. (FEMORAL)	PULSE PR. (FEMORAL)	MAXIMAL EJECTION PERIOD	REDUCED EJECTION PERIOD	TOTAL SYSTOLE
1182	317	+	155/85	70	0.08	0.16	0.24
1181	309	+	165/80	85	0.08	0.14	0.22
1199	305	+	200/110	90	0.08	0.14	0.22
1217	289	+	175/105	70	0.08	0.12	0 20
1193	282	+	150/105	45	0.06	0.10	0.16
1231	272	–	150/95	55	0.06	Absent Dicrotic Notch	
1238	259	+	200/100	100	0.06	0.12	0.18
1330	173	+	135/100	35	0.06	0.12	0.18
1358	167	+	165/90	75	0.06	0.16	0.22
1359	26	+	85/55	30	0.06	0.12	0.18
1372	60	+	165/110	55	0.06	0.12	0.18

needle was passed percutaneously into the left ventricle at the point of maximal impulse, usually the fifth intercostal interspace A polyethylene catheter of appropriate size was threaded through this needle into the ventricle and then through the bicuspid aortic valve into the central aorta Proper connections were made to Statham strain gauges P23A and a Sanborn Poly Viso recorder with recording speed of 25 mm per second

RESULTS

Analyses of femoral artery pulse curves (Table I and Fig 6) show the presence of dicrotic notches in ten of eleven studies Several animals showed broadened pulse pressures Significant alterations in the duration of systolic ejection phases were not found

Continuous pressure recordings from the central aorta to the left ventricle (Table II and Fig 7) show a minor systolic gradient in 4 animals End diastolic pressures were slightly elevated in 2 animals

TABLE II CONVERSION OF TRICUSPID AORTIC VALVE TO BICUSPID VALVE
CENTRAL AORTIC AND LEFT VENTRICULAR PRESSURES
CHRONIC STUDIES 80 405 DAYS POSTOPERATIVE

ANIMAL NO	DAYS POSTOP	PRESSURE MM Hg						
		CENTRAL AORTA	LEFT VENTRICLE	SYSTOLIC AORTIC VALVE GRADIENT	END DIASTOLIC LEFT VENTRICLE	CENTRAL AORTIC PULSE	MEAN	
							CENTRAL AORTA	LEFT VENTRICLE
1182	405	125/100	125/0 13	0	0 13	25	115	55
1181	344	135/100	135/0	0	0 5	35	100	83
1199	344	100/75	140/0	40	0	25	90	55
1217	374	125/95	125/5	0	5	30	100	45
1193	321	110/75	120/–5	10	–5	35	100	65
1231	317	100/80	135/0 15	35	0 15	20	90	50
1238	317	110/85	125/0	15	0	25	85	50
1330	211	80/45	80/0 5	0	0 5	40	55	33
1358	221	160/130	165/0	5	0	30	135	100
1359	80	100/80	95/0 5	–5	0 5	20	90	50
1372	114	115/90	115/0	0	0	25	105	50

Since the completion of these studies (90+ days) the animals continue to be well, displaying normal activities for caged subjects

DISCUSSION

Acute and chronic studies demonstrate that dogs tolerate plastic revision of the aortic tricuspid valve to a bicuspid valve Pathologic studies as shown in the manuscript support the feasibility of this concept and method for *clinical application in the surgical treatment of aortic insufficiency* More recent studies by us, employing hydraulic and cinephotographic studies as described by McMillan,[3] show that (1), at least in rheumatic aortic valvular insufficiency, the noncoronary aortic cusp appears to interfere with the coaptation of all three cusps and accordingly contributes to the pathogenesis of the regurgitation, and (2) the reconstructed bicuspid aortic valve in the same diseased specimens coapts remarkably well and minimizes regurgitation

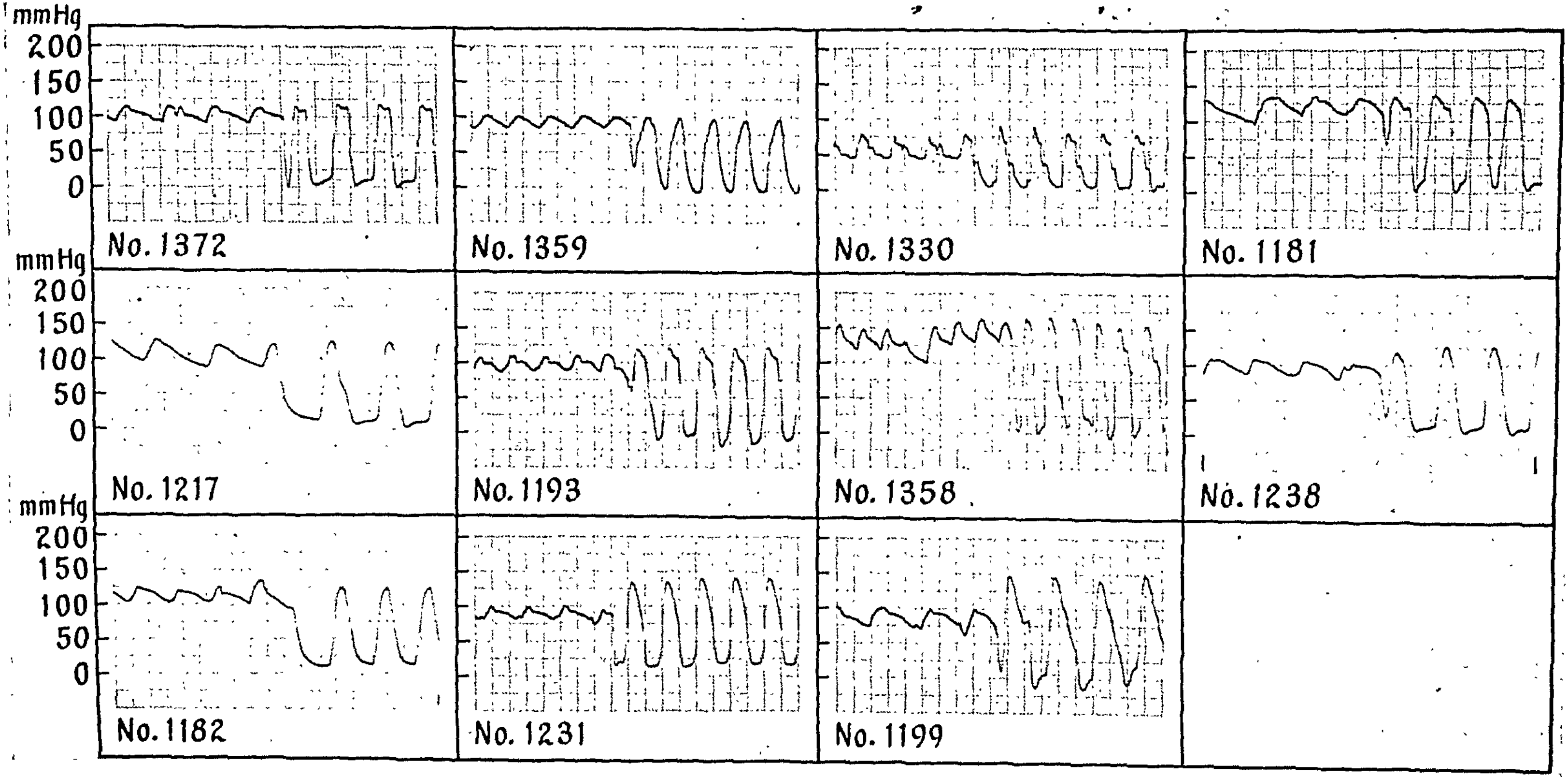

Fig. 7.—Conversion of tricuspid aortic valve to bicuspid valve. Continuous pressure curves from central aorta and left ventricle. Chronic studies 80-405 days postoperative.

SUMMARY

1. A method of aortic valvuloplasty, conversion of the tricuspid aortic valve to a bicuspid valve, is described for the surgical treatment of aortic insufficiency.

2. Chronic experimental studies demonstrate the canine tolerance for the procedure.

3. Pathologic and cinephotographic studies support the clinical application of the concept and method.

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HYPOTHERMIC ANALGESIA FOR OPEN HEART SURGERY WITH THE HEART-LUNG MACHINE

William W. Musicant, M.D., Reuben R. Lewis, M.D., C.M., Belmont S. Musicant, M.D., Robert M. Anderson, M.D., and Jerome Harold Kay, M.D., Los Angeles, Calif.

EXTRACORPOREAL circulation is an accepted technique used to facilitate and make possible the surgical correction of formerly incurable congenital and acquired cardiovascular lesions.[1] This surgical advent has brought about certain exigencies in the field of anesthesia about which little has been reported. In the studies that have been made and reported of anesthesia during extracorporeal circulation,[2] the use of depressant anesthetics and hypnotics is advocated before and during the period of cardiopulmonary bypass.[2] Patients requiring extracorporeal circulation for correction of disease must be classed as "poor risk" and therefore do not tolerate depressant drugs or hypoxia very well. Light planes of anesthesia frequently produce arrhythmias and persistence to deeper planes many end disastrously. To facilitate surgical intervention in such patients, the use of anesthetic adjuncts, such as muscle relaxants,[3] hypothermia,[4] analgesic planes of potent anesthetics,[5] and hypnosis[6] has come into vogue. All of these have finite salutary attributes and these effects have been incorporated into one technique and utilized during the various stages of any one operation. Such a combined technique most closely approximates the "ideal" of the perfect anesthetic for these "poor risk" patients. It must be remembered, however, that one of the most critical periods of open heart surgery is that of cardiopulmonary bypass. It is during this period that paucity of drug effect is most desirable. With that end in view, an analgesic level of hypothermia was postulated. It was felt that such a state would obviate the use of depressant drugs in order to maintain satisfactory operating conditions during bypass.

In 1950, Bigelow and associates[7] pointed out that animals cooled below 28° C. entered a state of "cold narcosis" during which an anesthetic agent was no longer necessary for maintaining unconsciousness and relaxation. In 1950, McQuiston[8] showed that surgical correction of congenital heart conditions is more safely performed with the patient's temperature reduced.

From the Department of Surgery of the University of Southern California School of Medicine, Saint Vincent's Hospital, California Hospital Babies and Children's Clinic, Los Angeles, Calif.

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Under hypothermia, adrenal stress reactions are both reduced and delayed, and patients who are operated on under those conditions do not demonstrate the usual retention of water and salt during the early postoperative period.[9] Moderate hypothermia (30°-32° C.) lowers cerebral metabolism from 75 to 40 per cent.[10] Virtue[11] has stated that with a reduced cerebral metabolic rate, a smaller amount of anesthetic is required to obtain surgical anesthesia. Ventricular fibrillation is more difficult to treat in the hypothermic state and at esophageal temperatures of 28° C. or below, ventricular fibrillation is more apt to occur. Recently, experimental evidence has been accumulating that the cholinomimetic agent, succinylcholine, not only has fine muscle relaxing qualities but also blocks the cardiac effects of sympathetic and parasympathetic stimulation by depolarization.[12]

Two methods of producing hypothermia are now being employed.[13] The most frequently used method consists of surface cooling. The patient is first anesthetized and then immersed in an ice water bath or covered with ice bags. The other method consists of utilizing extracorporeal circulation to produce hypothermia. A method of open heart surgery utilizing extracorporeal circulation and producing analgesic level of hypothermia has been employed and found to be most satisfactory.

METHODS

The Kay-Anderson pump oxygenator* (Fig. 1) was used for all of these operations. The apparatus is operated by one person and is capable of oxygenating and pumping 6 L. or more of blood per minute. Metabolic acidosis does not occur during cardiopulmonary bypass. Nine units of blood are used in the apparatus during the procedure. The blood is oxygenated by blowing 10 L. of 97.5 per cent oxygen and 2.5 per cent carbon dioxide across the filming screens. During the procedure the aortic pressure is monitored and maintained at a relatively normal mean pressure. The electrocardiogram is also monitored. A thermocouple lead is placed in the lower third of the esophagus for constant temperature readings. Blood volume studies are done before and after surgery. The blood used in the machine is approximately 5 hours old and is placed in a water bath at 38° C. 1 hour prior to filling the pump oxygenator. However, the oxygenator, which is made of stainless steel, is not warmed prior to adding the blood or during bypass. This accounts for the sustained hypothermia until the end of cardiopulmonary bypass.

In order to avoid any possible deleterious effect on the cardiovascular system, no preoperative medication is given. Cyclopropane and/or ether is used for all inductions. The younger patients are induced with open cyclopropane and the older patients with a closed circle system. Following induction venous cutdowns are performed. After tracheal intubation, all patients are put on a semiclosed system employing nitrous oxide and oxygen and are given a slow continuous drip of succinylcholine (Anectine). The thoracotomy incision is made by one team while a separate team isolates both femoral arteries. After the femoral vessels are isolated, this team completes the opening of the left chest, while the other team completes the opening of the right chest. As soon as both sides of the chest are entered, manually controlled respiration is instituted and maintained until the chest is closed again. As soon as extracorporeal circulation is started and during the intracardiac repair, the drip rate of succinylcholine (Anectine) is doubled. A mixture of 40 per cent oxygen and 60 per cent helium is used to inflate the lungs gently 5 to 10 times per minute during bypass. This is done to ensure adequate oxygenation of alveolar epithelium[14] and to prevent unresolvable atelectasis.

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*Constructed by Corço Incorporated, 10418 Venice Boulevard, Los Angeles 34, Calif., for Dr. Kay and Dr. Anderson.

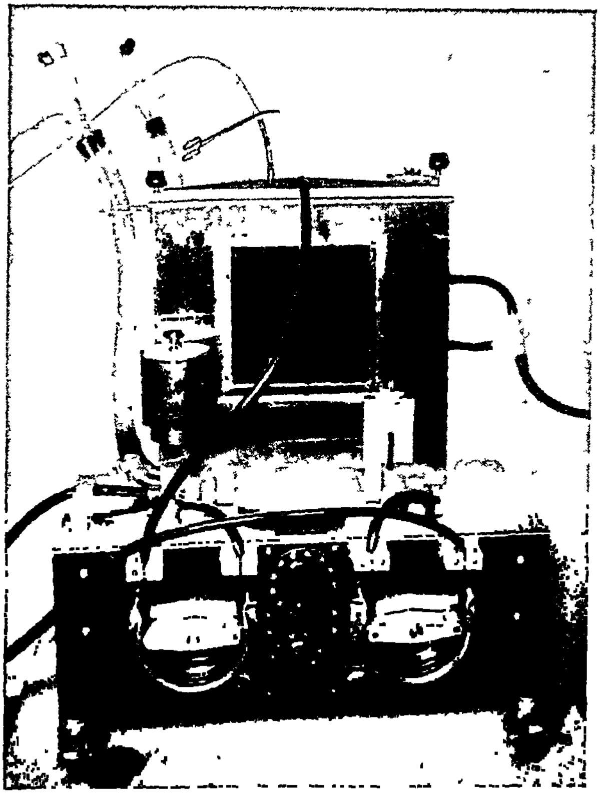

Fig. 1.—The Kay-Anderson autoclavable stainless steel heart-lung machine

Immediately upon going on bypass, there is a sudden drop in body temperature as measured by the esophageal lead (Fig. 2). This drop continues for the next 3 minutes and levels off after 2 more minutes between 31° and 31.5° C. This temperature is sustained during the entire time that extracorporeal circulation is maintained. During this time, no attempt is made to introduce any anesthetic drug other than to keep all striated muscle paralyzed with succinylcholine. Upon completion of bypass, the succinylcholine drip is completely discontinued and 50 per cent nitrous oxide and 50 per cent oxygen is started. This mixture is maintained until completion of the surgery. Following cardiopulmonary bypass, no other drug or agent is required to keep the patient anesthetized. Also, during this period, the temperature gradually rises (Fig. 2) and at the end of surgery is only 1° to 2° C. below normal. No attempt is made to warm the patients artificially. At the completion of the operation and upon discontinuance of the nitrous oxide, all of the patients are awake.

RESULTS

Fifteen patients underwent surgical correction of their cardiac defects using this technique (Table I) and all reacted identically, with one exception This patient had a prolonged succinylcholine effect He was awake at the end of surgery, however, he required assisted respirations for about 30 minutes postoperatively

In spite of the fact that preoperative drying agents were not used, respiratory secretions were not a problem The usual cardiac slowing, seen under hypothermia, was not encountered in any of the cases

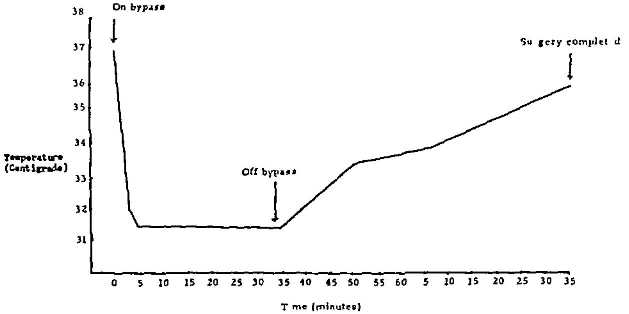

Fig 2—Time Temperature Chart Case 1—on cardiopulmonary bypass 32 minutes

The types of surgery and the ages of the patients are shown in Table I With the exception of Case 4, all patients did extremely well postoperatively Case 4 died 18 hours after surgery Although precautions were taken in an attempt to prevent cardiac tamponade, a thick clot formed around the heart and produced cardiac tamponade The patient was alert until shortly before death Necropsy revealed the tamponade and excellent closure of the interatrial and interventricular septal defects Since then the pericardial sac has not been closed

The length of time of bypass varied from 16 minutes to 42 minutes Careful questioning of all patients revealed that no one had any recollection of any part of the surgery All patients remembered going to sleep and the younger patients remembered only the stories they were told during the induction

COMMENT

In planning this anesthetic technique, drugs that might have a deleterious effect on the myocardium were avoided By warming the heparinized blood to 38° C prior to filling the machine, and not warming the stainless steel oxygenator, an almost constant time temperature reduction could be predicted The temperature fall did not appear to be related to the weight of the patient or the time on bypass, after the first 5 minutes This allowed us to arrive at levels of "Hypothermic Analgesia" At these levels (31° to 32 5° [illegible] an[illegible]ic

TABLE I. ANALYSIS OF FIRST 15 PATIENTS UNDERGOING INTRACARDIAC SURGERY UTILIZING HYPOTHERMIC ANALGESIA

PATIENT	DATE OF OPERATION	AGE (YEARS)	WEIGHT (LBS.)	DIAGNOSIS	PROCEDURE	OUTCOME
1. K. H.	12-12-57	8	70	Ventricular septal defect	Closure of defect	Lived; defect completely closed
2. J. F.	1- 9-58	8	40	Ventricular septal defects	Closure of defects	Lived; defects completely closed
3. A. V.	1-16-58	8	50	Patent ductus arteriosus and ventricular septal defects	Ligation of ductus and closure of defects	Lived; defects completely closed
4. D. L.	1-30-58	4	28	Atrial septal defect and ventricular septal defect	Closure of atrial and ventricular septal defects	Died 18 hours postop. of cardiac tamponade; both defects completely closed
5. R. C.	2- 6-58	8	70	Atrial septal defect and valvular pulmonic stenosis	Closure of atrial septal defect and pulmonary valvulotomy	Lived; defects completely treated
6. A. DeL.	2-20-58	7	50	Patent ductus arteriosus and tetralogy of Fallot	Ligation of ductus, resection of infundibular stenosis and closure of ventricular septal defect	Lived; defects cured
7. R. M.	2-27-58	2	29	Patent ductus arteriosus and ventricular septal defect	Defect closed and ductus ligated	Lived; defects completely closed
8. N. P.	3-12-58	4½	38	Ventricular septal defect	Closure of defect	Lived; defect completely closed
9. D. S.	3-20-58	4¾	39	Ventricular septal defect	Closure of defect	Lived; defect completely closed
10. S. H.	3-27-58	7	40	Patent ductus arteriosus and ventricular septal defects	Ductus ligated and defect closed	Lived; defects completely closed
11. D. S.	4- 3-58	6	45	Ventricular septal defect	Closure of defect	Lived; defect completely closed
12. R. J.	4-17-58	2¾	32	Ventricular septal defect	Closure of defect	Lived; defect completely closed
13. B. J.H.	4-28-58	8	40	Ventricular septal defect	Closure of defect	Lived; defect completely closed
14. L. A. E.	5- 7-58	3	30	Ventricular septal defect	Closure of defect	Lived; defect completely closed
15. W. T.	5-22-58	23	143	Ventricular septal defect	Closure of defect	Lived; defect completely closed

was necessary Muscular movement of the patients was controlled and untoward cardiac reflexes did not occur This was probably due to the succinylcholine

SUMMARY

A new concept of hypothermic analgesia for extracorporeal open heart surgery is presented Except for a muscle relaxant, no other anesthetic adjunct was required to maintain surgical anesthesia during bypass Fifteen cases are reported with only one mortality and the technique is described

ADDENDUM

The authors now use a median sternotomy instead of a bilateral anterior thoracotomy

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THE EFFECT OF PROLONGED VENO-ARTERIAL PUMPING ON THE CIRCULATION OF THE DOG

Neil A. J. Hamer, M.B., M.R.C.P., James F. Dickson III, M.D.,* and James W. Dow, M.D.,* Boston, Mass.*
*With the Technical Assistance of Carl E. Hewson.***

INTRODUCTION

The volume work of the heart may be reduced by diverting part of the venous return and pumping it into the aorta. Such veno-arterial shunting may prove to be beneficial for days following myocardial infarction or pulmonary embolism. The purpose of this study is to determine the long-term effects of pumping a large proportion of the venous return into the aorta on cardiac output, regional oxygen supply, clotting mechanism, and acid-base balance.

METHODS

The technique and equipment for veno-arterial shunting are described in detail in a separate report. Blood flows by gravity through a cannula with tip placed at the junction of the superior vena cava and the innominate veins into a collecting chamber or plastic bag, and is pumped from there to the bifurcation of the aorta by way of a cannula in a femoral artery (Fig. 1). The pump is pneumatically cycled with ball-valves at each end of the pumping element.†

An open collection system with weir flow-meter was used for the first eleven procedures. A closed plastic bag was substituted for the open chamber in the last four experiments. Flows were calculated from time collections of 100 c.c. of blood in the chamber or 100 grams in the bag. The closed system was air-free and tightly distended with 800 to 1,100 c.c. of freshly drawn, heparinized, homologous donor blood before the bypass was started. Temperature was controlled by warming a loop of the arterial line in a water bath except in the first two experiments.

From the Tufts Medical Services, Circulation Laboratory and Thoracic Surgical Services, Boston City Hospital, and the Departments of Medicine and Surgery, Tufts University School of Medicine, Boston, Mass.

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*Present address: The Presbyterian Hospital, Philadelphia, Pa.

**Of the Brunswick Manufacturing Co., Quincy, Mass.

†Built by the Brunswick Manufacturing Co., Quincy, Mass.

Polyethylene catheters were placed with their tips in the intrathoracic inferior vena cava, at the arch of the aorta, and in the aorta at diaphragm level. Samples drawn from these locations and from the bypass line were analyzed for oxygen content and saturation, carbon dioxide content, pH, hematocrit, electrolytes, and clotting factors. Blood buffer base and pCO_2 were derived from the Singer-Hastings nomogram.[1] Control arteriovenous differences were calculated from the formula:

$$\text{AV difference} = A - \frac{1}{3}(S + 2I)$$

where A = arterial oxygen content
S = superior vena caval oxygen content
I = inferior vena caval oxygen content

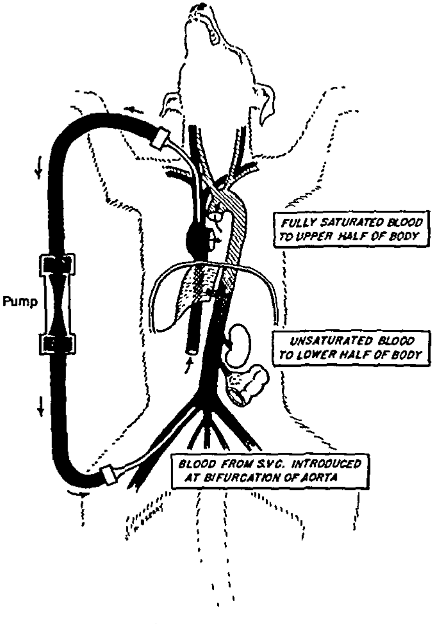
FULLY SATURATED BLOOD TO UPPER HALF OF BODY
Pump
UNSATURATED BLOOD TO LOWER HALF OF BODY
BLOOD FROM S.V.C. INTRODUCED AT BIFURCATION OF AORTA

Fig. 1.—Unsaturated blood is withdrawn from the superior vena cava and pumped into the aorta at the bifurcation to perfuse the legs, back, and lower abdomen. The oxygen saturation of blood supplying the heart, brain, and upper abdomen is unaffected.

When the bypass flow was greater than 30 c.c./Kg./min. the pulmonary arteriovenous difference was calculated from the upper aortic and the inferior caval oxygen contents. In one experiment, the cardiac output during perfusion was estimated from the change in pulmonary arteriovenous oxygen difference, assuming that the oxygen consumption was constant. The presence of hemolysis

TABLE I. EFFECTS OF VENO-ARTERIAL SHUNTING: 22 TEST PERIODS IN 9 ANIMALS

CONTROL VALUES	DOG NO.	BLOOD PRESSURE SYST. | DIAST. (MM. Hg)	BODY TEMPERATURE (DEGREES C.)	VOLUME OF VENO-ARTERIAL SHUNT (C.C./Kg./MIN.)	OXYGEN SATURATION (%)				PULMONARY ARTERIO-VENOUS O_2 DIFFERENCE (C.C./L.)	ARTERIAL pCO_2 (MM. Hg)	BUFFER BASE (mEq./L.)
					AORTA						
					ARCH	DIAPHRAGM LEVEL	BYPASS LINE	IVC			
Mean		178/132	37.7		98	99	85	72	37	36	45
Upper limit		240/165	38.3		103	104	92	78	46	45	50
Lower limit		130/100	37.0		89	94	79	62	23	27	41
	2	130/100	37.8	25	102	107	86	86	36	--	--
	4	160/145	37.1	26	93	92	66	50	--	--	--
	2	130/100	36.2	28	97	102	87	79	44	--	40
	3	200/155	37.6	33	93	101	78	70	62	--	--
	14	180/150	36.0	34	--	110	91	72	76	34	40
	13	210/160	37.8	34	--	88	76	52	73	57	38
	14	240/150	38.0	36	--	86	74	59	57	32	40
	14	220/120	37.8	36	--	110	66	51	91	33	36
	1	140/95	37.4	38	99	100	73	--	--	26	52
	3	200/160	38.1	42	99	98	88	65	73	--	--
	4	175/145	35.0	43	94	99	61	48	113	--	--
	15	165/120	36.4	43	--	107	57	46	106	34	33
	5	150/115	37.0	45	98	93	83	67	55	32	47
	5	160/130	36.2	45	94	97	85	65	75	44	45
	15	150/100	37.4	46	--	95	69	58	55	50	31
	15	160/100	37.6	46	--	99	75	48	67	34	30
	3	205/170	38.0	53	100	94	77	58	86	--	--
	4	165/140	34.6	54	101	98	57	50	114	30	46
	15	170/120	38.0	57	--	110	59	42	77	28	30
	3	200/165	38.2	63	97	77	74	54	93	18	47
	7	145/110	37.6	64	93	102	52	37	124	33	45
	7	170/140	37.7	71	101	100	55	40	126	37	45

was detected by inspection of the plasma in hematocrit tubes after centrifuging. Aortic pressure was constantly recorded on direct-writing paper using a P23Db strain gauge and Sanborn 67 series Poly-Viso.

The last 9 bypasses were started at a rate of 100 to 200 c.c. per minute for 10 minutes before full flow was attempted. When a pronounced drop in arterial pressure occurred during the initial blood exchange, bypass was stopped and the animal allowed to recover for 30 to 45 minutes before bypass was resumed at full flow.

Indicator dilution curves were recorded on direct-writing paper using indigo carmine dye and a Colson constant-flow densimeter system. Dye was injected into the inferior vena cava and the concentration recorded in blood from the aortic arch.

Blood for priming the system and replacement of loss was drawn from donor animals by exsanguination under light Pentothal anesthesia. The heparin concentration in the collection bottles ranged from 23 to 51 mg. per liter. Donor and subject animals were cross-matched in the last three experiments. The subject animal was lightly anesthetized with Pentothal and maintained with 25 to 75 mg. doses of Nembutal as required. The trachea was intubated and oxygen run in through a catheter at a flow of 2 L. per minute. The animals were allowed to breathe spontaneously. The total oxygen content of arterial blood is expressed as a percentage of hemoglobin capacity without correction for dissolved oxygen.

Each subject received 2 mg. per kilogram of body weight of heparin initially. Heparinization was maintained with doses of 50 to 100 mg. every 3 hours, except in the last experiment in which a continuous infusion was given.

Cineangiography was performed in 2 animals using a Phillips image intensifier and 16 mm. movie film. Ninety per cent Hypaque, at a concentration of 0.66 c.c. per kilogram, was injected into the femoral artery cannula during maximal bypass.

RESULTS

Fifteen animals were studied. In 6 animals, hypotension and normovolemic shock occurred a few minutes after the onset of veno-arterial pumping. Five of these were excluded from the analysis. The sixth animal recovered rapidly and, as final control samples were similar to those taken before the onset of shock, was included in the study. In 5 dogs, long-term perfusion was undertaken.

Effects of Veno-Arterial Shunting at Various Rates.—Twenty-two test periods in 10 animals were found suitable for evaluation. Six further test periods were excluded because of respiratory depression, uncontrolled cooling, or a diastolic blood pressure below 90 mm. Hg. The volume of the veno-arterial shunt ranged from 25 to 71 c.c./Kg./min. (Table I).

There was no significant change in mean arterial blood pressure during perfusion. However, the pulse pressure was considerably reduced with elevation of the diastolic pressure (Fig. 2).

The oxygen saturation of blood in the aorta at the arch and at the diaphragm was unchanged by veno-arterial pumping, except in one test period at 63 c.c./Kg./min. in which the oxygen saturation at the diaphragm fell to the level found in the shunt line.

The oxygen saturation of blood from the bypass line ranged from 79 to 92 per cent in the control samples, while the inferior vena caval saturation was between 62 and 78 per cent. With increasing veno-arterial pumping, both bypass line and inferior caval oxygen saturations tended to fall. In the 6 test periods with a bypass flow greater than 50 c.c./Kg./min., the bypass line saturation averaged 62 per cent and the inferior caval saturation 47 per cent (Fig. 3).

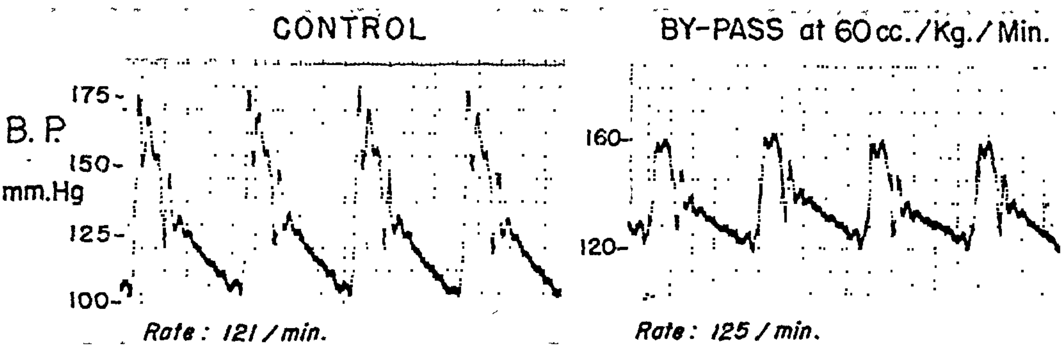

Fig. 2.—The effect of veno-arterial pumping on the aortic pressure pulse. During perfusion the pulse pressure is diminished and the diastolic pressure is elevated.

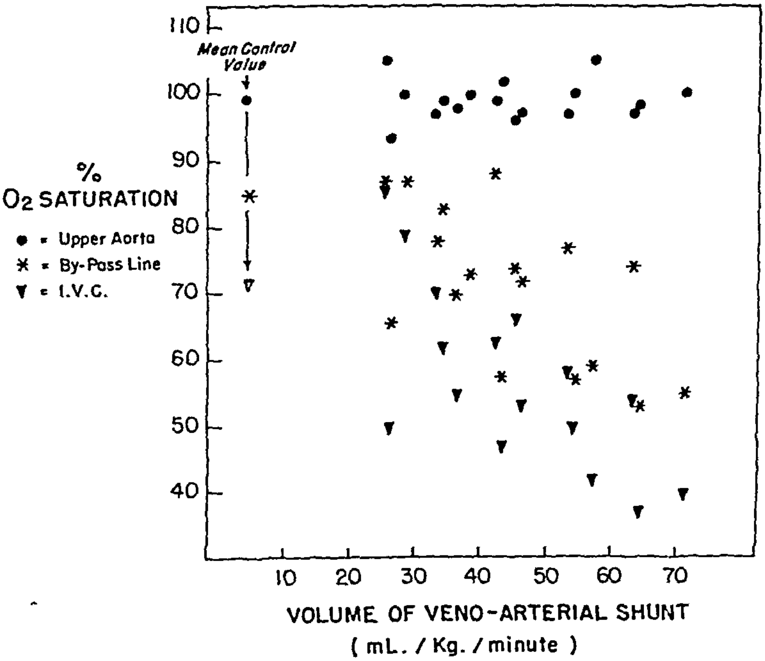

Fig. 3.—The oxygen saturation in the upper aorta is unaffected by veno-arterial shunting. The saturation in the bypass line and in the inferior vena cava falls progressively with increasing perfusion.

The pulmonary arteriovenous oxygen difference increased progressively with the volume of the veno-arterial shunt above values of 30 c.c./Kg./min.

(Fig 4) In Dog 3 the cardiac output was estimated during perfusion The sum of cardiac output and bypass flow was between 101 and 108 c c /Kg /min in four test periods The average cardiac output determined by the dye dilution method in 5 control periods was 105 c c /Kg /min

The arterial pCO_2 showed little change The buffer base was normal in the control period and was not consistently affected by veno arterial pumping The low values in Dog 15 were attributed to hemorrhage (Table I)

Cineangiography with bypass flows of 58 and 60 c c /Kg /min showed that the shunt blood filled the aorta and its branches to just below the level of the diaphragm The upper level of the opacified blood fluctuated with the heartbeat The renal and hepatic arteries were filled with dye blood only during ventricular diastole (Fig 5)

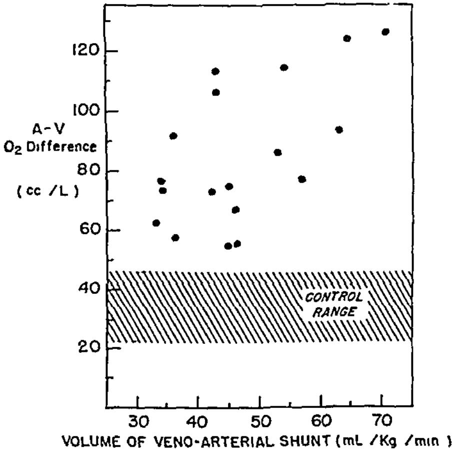

Fig 4 —The arteriovenous oxygen difference across the lungs increases with the bypass flow indicating a progressive reduction in the output of the heart

Prolonged Veno Arterial Shunting—Long term studies were undertaken in 5 animals (Table II) In 4, the procedure was terminated by the death of the animal Dog 14, however, survived after 52 hours' perfusion

Table II

DOG NO	VOLUME OF VENO ARTERIAL SHUNT (C C /KG /MIN)	DURATION OF SATISFACTORY PERFUSION (HOURS)	TOTAL DURATION OF PERFUSION (HOURS)	CAUSE OF TERMINATION OF PROCEDURE	MEAN DOSE OF HEPARIN (MG /KG / HR)
2	25	14	19	Uncontrolled cooling	0 58
3	42	16	17	Aspiration of vomit	0 68
5	44	13	24	Probable incompatible transfusion	0 81
14	36	52	53	Occlusion of pump by clot	1 18
15	45	35	39	Continued blood loss	1 60

In the first experiment, uncontrolled fall in body temperature to 32° C. was associated with a fall in blood pressure and blood oxygen content, and eventual death after 19 hours. In subsequent animals, normal body temperatures were maintained. In Dog 5, a fall in blood pressure and oxygen saturation after 13 hours followed transfusion from a new donor. The next experiment was satisfactory for 52 hours when the pump became occluded by a thrombus (Fig. 6). The animal recovered rapidly from the anesthetic and no untoward aftereffects were noted. The final dog (No. 15) was difficult to manage because of continued hemorrhage from operation sites.

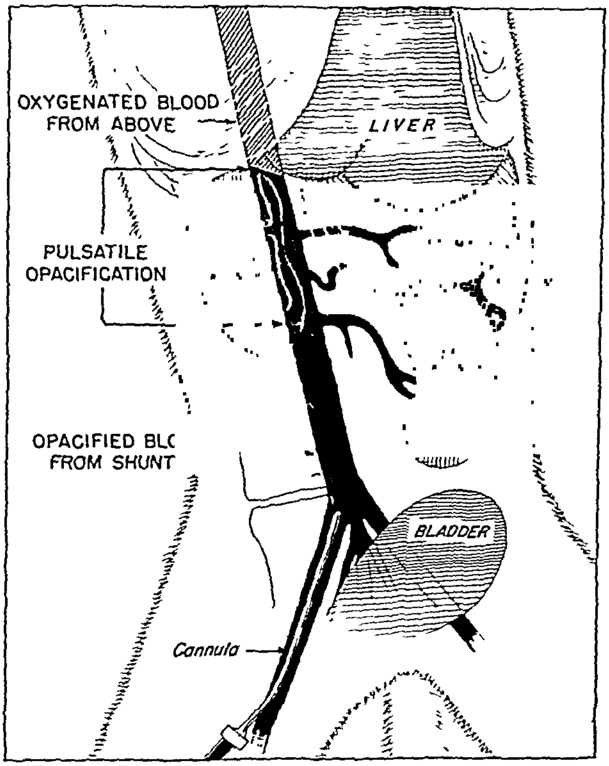

Fig. 5.—This diagram is constructed from a cineangiographic study in which the bypass flow was opacified. At a shunt flow of 60 c.c./Kg./min. unsaturated blood reaches the level of the diaphragm. Ventricular systole, however, fills the renal and hepatic arteries with fully saturated blood.

During these prolonged experiments, a normal urine volume was maintained, and the blood nonprotein nitrogen rose only from an average of 22 to 31 mg. per 100 c.c. The electrolyte pattern of the plasma was little disturbed.

Effect of Prolonged Pumping on the Coagulation Mechanism.—In the first three experiments the changes were uniform. The fibrinogen content was little affected, and the measurements of prothrombin, proconvertin, and Stuart factor, together with the Quick "prothrombin" time, showed moderate prolongation (Fig. 7). The platelet count fell in the first hour to approximately 100,000 per cubic millimeter, but showed no subsequent change. In the fourth dog, there were similar changes until the forty-eighth hour when the platelet count fell to 40,000 per cubic millimeter and the fibrinogen to 227 mg. per 100 c.c. Clotting in the apparatus was noted a few hours later. In the fifth animal, a larger

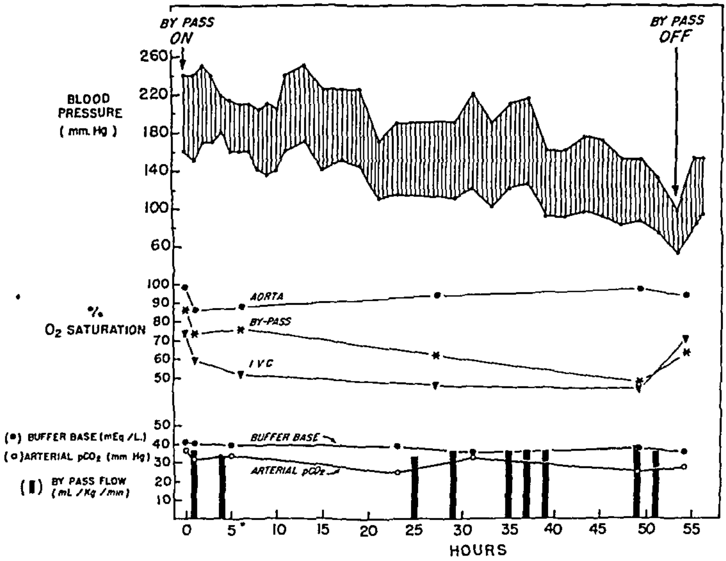

Fig 6 —Dog 14 was perfused at 36 c c /Kg /min for 52 hours with survival The bypass was terminated when thrombus occluded the pump A fall in blood pressure at this time was due to temporary loss of blood into the collection bag

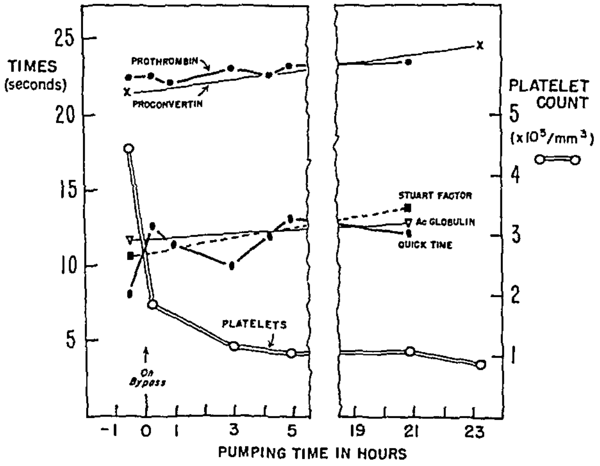

Fig 7.—Changes in coagulation factors during prolonged veno arterial shunting in Dog 5

over-all dose of heparin was given by continuous infusion and hemorrhage became a problem. The changes in coagulation factors were, however, similar to those in the previous experiments.

Hemolysis.—No consistent changes in hematocrit, hemoglobin, or red cell count were found. Hemolysis was noted in the first blood samples after the onset of perfusion in 5 of the 15 animals. In 3 of these 5, the apparatus had been primed with mixed blood from 2 donor dogs. Late hemolysis was found only in 3 animals in which blood from a second donor dog was used for transfusion after several hours.

DISCUSSION

At low rates of veno-arterial pumping, blood is drawn from the superior vena cava only, and is 70 to 80 per cent saturated with oxygen. This blood supplies the lower extremities. At shunt flows greater than 30 c.c./Kg./min., the rate of superior vena cava return is exceeded, and the shunt line draws increasingly from the inferior vena cava. At flows of 60 c.c./Kg./min., the shunt mixture is composed of roughly equal parts of superior and inferior caval blood. Part of the coronary sinus flow is presumably also drawn off. In consequence, the lower part of the body is perfused by progressively larger volumes of more reduced blood.

Most of this oxygen-poor blood goes to supply the muscle mass of the lower extremities and back. At shunt flows of 58 and 60 c.c./Kg./min., cineangiograms show the dyed interface to oscillate at mid-abdominal level in the aorta (see Fig. 5). The shunted blood fills the renal arteries and reaches as high as the celiac axis during diastole, but is forced back past the renal vessels by ventricular systole. The splanchnic bed is therefore perfused in large part by freshly oxygenated blood even at the highest veno-arterial flows attained.

Progressive widening of the arteriovenous oxygen difference across the lung provides evidence that cardiac output declines as the veno-arterial shunt increases (see Fig. 4), and suggests that total body perfusion remains constant. Experiment No. 3, in which the sum of bypass flow and cardiac output is similar to the control cardiac output determined by the dye dilution method, supports this conclusion.

In addition to saturation of arterial blood, oxygen availability is determined by the rate of blood flow and of oxygen utilization. In these experiments, total tissue flow is maintained, and arterial blood supplying coronary, cerebral, and most of the splanchnic beds is fully oxygenated at shunt volumes up to 50 c.c./Kg./min. The low saturation of the final venous mixture obscures the fact that contributions to this mixture from the vital organs cannot be poor in oxygen.

If total body perfusion is unchanged, the volume output of the heart is reduced quantitatively by the volume of the veno-arterial shunt. This reduction is reflected in the narrowed aortic pressure pulse (see Fig. 2). At the same time, the higher diastolic pressure should tend to increase the myocardial blood flow.

SUMMARY

1 A system for diverting part of the venous return from the venae cavae and pumping it into the aorta at the bifurcation has been devised

2 The maximum rate of pumping achieved was 71 c c /Kg /min , and the longest duration of satisfactory perfusion was 52 hours

3 Total tissue perfusion is not changed by pumping, so that the volume output of the heart is reduced by the amount of the shunt

4 The oxygen saturation of shunted blood falls progressively when the shunt is increased beyond 30 c c /Kg /min At flows from 50 to 71 c c /Kg /min , the oxygen saturation of shunted blood averages 62 per cent

5 Oxygenation of the splanchnic bed is normal at shunt flows less than 50 c c /Kg /min

6 Veno arterial pumping for 52 hours did not cause major irreversible changes in blood renal function, or acid base balance

Our thanks are due to Dr Herbert S Sise and his colleagues of the Anticoagulant Laboratory, Dr William C Moloney and Dr Jane Desforges of the Hematology Laboratory, Dr C Gardner Child III for the use of the apparatus for cineangiography, and Dr John J Byrne for the use of the facilities of the Boston University 3rd Surgical Research Laboratory at the Boston City Hospital also, to Miss JoAnn Harris for surgical assistance, Miss Faye Baer for the blood gas analysis, and Miss Violet Peters for her help in preparing the manuscript

ADDENDUM

This technique has recently been used to support the circulation in a patient with intractable congestive heart failure Veno arterial pumping was performed for 26 hours at a rate of 1 L per minute There was no evident change in the patient's condition as a result of the procedure, and he died 2 days later Autopsy showed no lesions attributable to the apparatus A striking feature was the plasma hemoglobin concentration which was only 5 mg per cent after 16 hours' pumping Evidence from the oxygen saturations suggests that the pumped blood was diverted to areas of low vascular resistance in the lower part of the body A larger extracorporeal flow might have been more effective Nevertheless, this experience demonstrates that veno arterial pumping is a practical procedure for use in man

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THE PHONOCARDIOGRAM AS A METHOD FOR EVALUATING MITRAL STENOSIS: CORRELATION WITH OPERATIVE FINDINGS

George L. Donnelly, M.D., George E. Maha, M.D., and
Edward S. Orgain, M.D., Durham, N.C.

IN RECENT YEARS, phonocardiography has been utilized to estimate the severity of mitral stenosis. The interval between the onset of electrical activation of the ventricle and the closure of the mitral valve (Q-1 interval), measured by means of simultaneous phonocardiogram and electrocardiogram, has been found usually to be prolonged in mitral stenosis.[1-4] Similarly, a shortened interval between the second heart sound and the characteristic opening snap of mitral stenosis (2-OS interval) has been thought to indicate the severity of the stenosis.[5] In mitral stenosis, these variations have been attributed to the pressure gradient across the mitral valve.[6, 7] It appears likely that, in predominant mitral stenosis, a delayed first sound results from elevation of left atrial pressure. Late equilibration of atrial and ventricular pressures during ventricular systole produces delayed closure of the mitral valve. Similarly, early equilibration of these pressures during the stage of isometric ventricular relaxation, because of elevated atrial pressure, would produce an early opening snap.

The diagnostic implications of prolongation of the Q-1 interval and of the time relationship between the second sound and the opening snap have led to investigations of the usefulness of these determinations in evaluating patients for mitral valve surgery. Bayer and associates[5] constructed a curve from simultaneous mean pulmonary capillary pressure and 2-OS intervals in 100 patients which roughly corresponded to the terminal slope of the ventricular isometric relaxation curve and indicated that the left atrial pressure could be thus estimated. Wells[6] examined a series of 30 patients and correlated the size of the mitral orifice at surgery with the Q-1 and 2-OS intervals and the difference between these intervals which he termed the Q-1 minus 2-OS value. Because of variations in these intervals with heart rate, he first analyzed a group with auricular fibrillation and found an approximate linear relationship between cycle lengths of 0.6 and 1.2 seconds for both the Q-1 and the 2-OS

From The Department of Medicine, Duke University School of Medicine, and The Cardiovascular Service, Duke Hospital, Durham, N. C.

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intervals. He thus was able to find "corrected" values for a cycle length of 0.8 second. Apparently using multiple observations in cases of sinus rhythm, he obtained corrected values in these cases also. The best correlation was thought to exist between mitral valve size and the "corrected" Q-1 minus 2-OS value. He thought that any delay in the individual intervals resulting from rigidity of the valve cusps would be offset by using both intervals for estimate.

The present study was undertaken to evaluate independently the usefulness of these determinations in the selection of patients for surgery.

METHOD

Forty-seven patients were studied by means of preoperative phonocardiograms. Estimations of valve size were made in each instance by the same surgeon* by means of insertion of the finger tip into the valve orifice at time of surgery. Intervals were measured from logarithmic phonocardiographic tracings taken at the apex and simultaneous Lead II electrocardiograms using a Sanborn Twin-Beam Cardiette. The Q-1 interval was measured from the onset of the QRS complex to the first major vibration of the first heart sound. The 2-OS interval was measured from the beginning of the second heart sound to the onset of the opening snap. Opening snaps were recorded in all but 3 patients. No patients had bundle branch block or discernible intraventricular conduction delay which might prolong the Q-1 interval.[3] One patient had 2:1 atrioventricular block.

Fifteen of the 47 patients had auricular fibrillation. Of these, 13 had detectable opening snaps. Assuming a linear relationship between the time intervals and the change in preceding cycle length between cycle lengths of 0.6 to 1.2 seconds, linear regression lines were calculated. Statistically significant values for the slope of these lines were obtained only when variation in cycle length exceeded 0.3 second. Such a range is required to produce measurable variations in the time intervals. The "corrected" Q-1 and 2-OS values could be calculated by substitution in the individual cases.

The mean regression coefficient with standard error was -0.048 ± 0.004 for the Q-1 intervals and 0.054 ± 0.004 for the 2-OS intervals. These figures for linear regression are essentially in agreement with Wells's observations of a decrease in Q-1 of 0.03 second and an increase in 2-OS of 0.03 second with change in cycle length from 0.6 to 1.2 seconds.

In our experience, regression lines could not be calculated in patients with normal sinus rhythm because of the narrow variations in cycle length. In those cases, after obtaining the means of multiple Q-1 and 2-OS intervals, correction of the intervals to a cycle length of 0.8 second was made by assuming a decrease of 0.005 second in Q-1 time and an increase of 0.005 second in 2-OS time for each increase of 0.1 second in cycle length. The validity of these corrections may be open to question.

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*Dr. Will Sealy, Professor of Thoracic Surgery.

Postoperative studies were carried out on 17 patients, 7 of whom had auricular fibrillation.

RESULTS

For general assessment, the patients have been grouped into four categories based on valve sizes of less than 0.5 cm.^{2}, 0.5 to 1.0 cm.^{2}, 1.0 to 1.5 cm.^{2}, and greater than 1.5 cm.^{2}.

Estimates of insufficiency and calcification were also made at operation. Scattergraphs (Figs. 1, 2, 3) show the correlation between the "corrected" Q-1 intervals, 2-OS intervals, and Q-1 minus 2-OS values and the mitral valve size at surgery. The Q-1 interval failed to disclose satisfactory predictive correlation with valve size. With five exceptions, the Q-1 interval was 0.07 second or greater in each of the valve size groups, and was 0.08 second or greater in 8 of 13 patients whose valve size was greater than 1.0 cm.^{2}.

However, reasonably good correlation is apparent for both the 2-OS interval and the Q-1 minus 2-OS value. Twenty-nine (85 per cent) of 34 patients, whose valve areas measured 1.0 cm.^{2} or less, had a 2-OS interval of 0.09 second or less in comparison to 2 of 10 patients whose valve size exceeded 1.0 cm.^{2}. All 11 patients whose valve area was less than 0.5 cm.^{2} exhibited a 2-OS interval of 0.09 second or less, as well as 18 of 23 patients whose valve size ranged from 0.5 to 1.0 cm.^{2}. Eight of 10 patients in whom the estimated valve size was greater than 1.0 cm.^{2} showed a 2-OS interval of 0.095 second or greater. Thirty (90 per cent) of 34 patients, whose valve area measured 1.0 cm.^{2} or less, exhibited Q-1 minus 2-OS values of −1.0 or greater, as compared to 3 of 10 patients whose valve size exceeded 1.0 cm.^{2}. Utilizing values of 0.09 second for 2-OS interval and −1.0 for Q-1 minus 2-OS difference, seven errors in prediction of valve size are noted for each of these indices employed alone. The estimated valve size at operation was smaller in 5 patients and greater in 2 patients than predicted from the 2-OS interval. Valve size was smaller in 4 patients and larger in 3 patients than predicted from the Q-1 minus 2-OS value. Because of overlap, these 14 prediction errors involve only 9 patients. However, when the values for both indices were satisfied as criteria of valve size, prediction errors remained in only 5 of the group of 44 patients; valve size was overestimated in 3 and underestimated in 2 patients.

The 17 postoperative studies showed changes in Q-1 and 2-OS intervals similar to those described by others.[3-6] The individual pre- and postoperative values in these cases are summarized in Table I. Five patients showed shortening of the Q-1 time compared to preoperative values while an additional 6 showed slight increases (Fig. 4). In 14 patients there was lengthening of the 2-OS interval (Fig. 5). Thirteen patients exhibited decreases in Q-1 minus 2-OS values, the change being greater in those patients presenting more severe mitral stenosis (Fig. 6). In 1 of the remaining 4 patients (Patient L. H.), pure mitral insufficiency was present and valvulotomy was not performed.

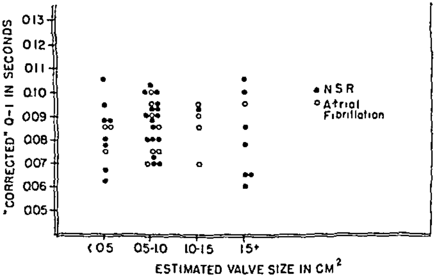

Fig. 1.—Scattergraph demonstrating relationship between estimated valve size and "corrected" Q-1

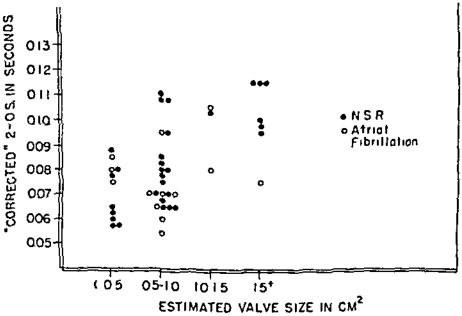

Fig. 2.—Scattergraph demonstrating correlation between valve size and "corrected" 2-OS.

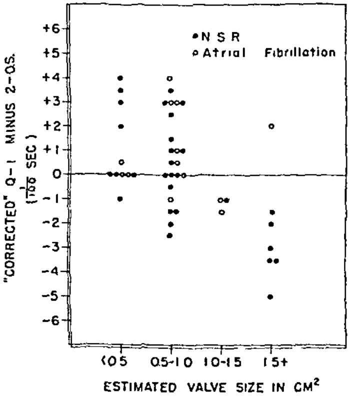

Fig. 3.—Scattergraph demonstrating correlation between estimated valve size and "corrected" Q-1 minus 2-OS.

TABLE I. COMPARISON OF PRE- AND POSTOPERATIVE VALUES FOR "CORRECTED" Q-1, 2-OS, Q-1 MINUS 2-OS INTERVALS AND VALVE SIZE

	BEFORE VALVULOTOMY					AFTER VALVULOTOMY				
PATIENT	RHYTHM	Q-1 IN SECONDS	2-OS IN SECONDS	Q 1 MINUS 2-OS	ESTIMATED VALVE AREA IN CM.²	RHYTHM	Q-1 IN SECONDS	2-OS IN SECONDS	Q-1 MINUS 2-OS	ESTIMATED VALVE AREA IN CM.²
L. B.	NSR	.088	.058	+3.0	0.5	NSR	.088	.068	+2.0	2.0
T. F.	Aur. Fib.	.085	.08	+0.5	0.5	Aur. Fib.	.085	.11	−2.5	3.5
H. C.	NSR	.088	.088	0.0	0.5	NSR	.09	.10	−1.0	1.0-1.5
F. B.	NSR	.08	.08	0.0	0.5	NSR	.083	.093	−1.0	2.5
D. D.	2:1 AVB	.10	.065	+3.5	0.5-1.0	2:1 AVB	.10	.08	+2.0	3.0
V. P.	Aur. Fib.	.10	.07	+3.0	0.5-1.0	Aur. Fib.	.075	.085	−1.0	3.5
V. H.	Aur. Fib.	.09	.06	+3.0	0.5-1.0	Aur. Fib.	.075	.11	−3.5	2.5
G. E.	NSR	.093	.078	+1.5	0.5-1.0	NSR	.085	.085	0.0	3.0
P. O'D.	NSR	.085	.075	+1.0	0.5-1.0	NSR	.093	.108	−1.5	3.0
L. P.	Aur. Fib.	.075	.065	+1.0	0.5-1.0	Aur. Fib.	.075	.065	+1.0	3.0
J. H.	NSR	.093	.083	+1.0	0.5-1.0	NSR	.10	.11	−1.0	3.0
C. B.	Aur. Fib.	.075	.07	+0.5	0.5-1.0	Aur. Fib.	.07	.085	−1.5	3.0
W. W.	NSR	.08	.08	0.0	0.5-1.0	NSR	.078	.093	−1.5	2.5
M. J.	NSR	.07	.085	−1.5	0.5-1.0	NSR	.085	.09	−0.5	3.5
J. S.	Aur. Fib.	.09	.105	−1.5	1.0-1.5	Aur. Fib.	.10	.12	−2.0	2.5-3.0
E. H.	Aur. Fib.	.095	.075	+2.0	1.5	Aur. Fib.	.095	.065	+3.0	3.0
L. H.	NSR	.065	.10	−3.5	4.0	NSR	.065	.10	−3.5	4.0

NSR—Normal sinus rhythm; Aur. Fib.—Auricular fibrillation; AVB—Atrioventicular block.

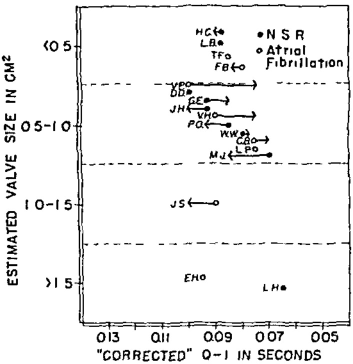

Fig. 4.—Individual changes in Q-1 values after operation (patients grouped according to valve size).

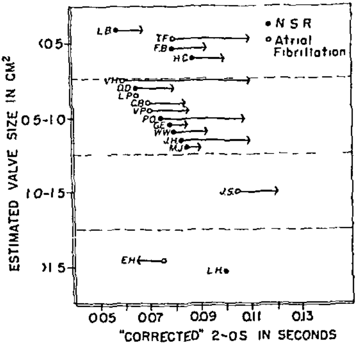

Fig. 5.—Individual changes in 2-OS values after operation (patients grouped according to valve size).

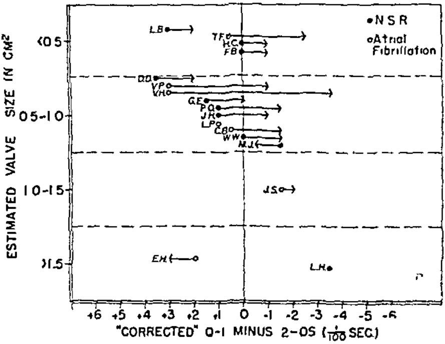

Fig 6.—Individual changes in Q-1 minus 2-OS values after ing to valve size).

DISCUSSION

The duration of the Q-1 interval failed to reveal appreciable correlation with valve size in this series. These observations are not in agreement with conclusions of others. Kelly[3] felt that, in the absence of bundle branch block, prolongation of the Q-1 interval was found *only* with *mitral stenosis* and that *a Q-1 interval of 0.07 second or more* indicated significant stenosis. Such a Q-1 interval range would encompass all save 5 patients in our entire group whose valve sizes varied from less than 0.5 cm.^{2} to greater than 1.5 cm.^{2}. Moreover, 8 of 13 patients who presented valve areas greater than 1.0 cm.^{2} had Q-1 intervals of 0.08 second or longer. Reasonably good correlation was found between valve size and the 2-OS interval. A short 2-OS interval, noted by most investigators in severe mitral stenosis, is thought to reflect elevated left atrial pressure.[3, 5, 6] An analysis of the scattergraph of our observations (Fig. 2) revealed that 29 (85 per cent) of 34 patients, whose valve areas measured 1.0 cm.^{2} or less, had 2-OS intervals of 0.09 second or less in comparison to 2 of 10 patients whose valve size exceeded 1.0 cm.^{2}. Each of the 11 patients whose valve area was less than 0.5 cm.^{2} had a 2-OS interval of less than 0.09 second. Steinzeig and associates[1] found less consistent shortening of the 2-OS interval but no comparisons were made with less severe cases or those without significant stenosis. This study demonstrates satisfactory correlation of mitral valve size with the Q-1 minus 2-OS value as noted by Wells.[6] Thirty (90 per cent) of 34 patients, whose valve areas measured 1.0 cm.^{2} or less, had a "corrected" Q-1 minus 2-OS value of –1.0 or greater as compared to 3 of 10 patients whose valve size exceeded 1.0 cm.^{2}. Six of 7 patients, whose valve size was greater than 1.5 cm.^{2}, had values more negative than –1.0. Wells[6] suggested that the use of the Q-1 minus 2-OS value would offset any prolongation of the Q-1 or 2-OS intervals caused by rigidity of the valve cusps. However, in our series, 6 patients with heavy valvular calcification showed no consistent lengthening of either interval over noncalcified cases with the same valve areas. Wells subsequently has reported on a group of 100 patients who had been studied preoperatively with phonocardiograms. In this group the mitral pressure gradient, determined at operation, was found to be high in patients who had a "corrected Q-1 minus 2-OS" greater than –1.5, while the pressure gradient was found to be low in patients who had a value less than –1.5.[8] Our determinations and correlation with valve size are in general agreement with those values.

In the group of patients considered, surgical intervention was decided mainly upon clinical grounds, sometimes assisted by right heart catheterization. With increasing use of left heart catheterization, phonocardiography may prove a useful adjunct to clinical evaluation. In patients suspected of having tight mitral stenosis, a "corrected" 2-OS interval of greater than 0.09 second and a "corrected" Q-1 minus 2-OS value more negative than –1.0 should lead to careful re-evaluation and, if necessary, left heart catheterization before surgery is undertaken. On this basis alone, 6 of the 7 patients, whose valve size at operation was found greater than 1.5 cm.^{2}, would now be recommended for left heart catheterization before surgery.

Recognizing significant agreement but with definite limitations, it appears that routine phonocardiography will assist in screening potential candidates for mitral valvulotomy. If the 2-OS interval is less than 0.09 second and the Q-1 minus 2-OS value is greater than -1.0 in the same patient, the likelihood of a fairly tight mitral stenosis is good. These indices, used together as criteria of valve size, possess greater value than either index used alone.

SUMMARY

The value of phonocardiography in selecting candidates for mitral commissurotomy has been assessed in a series of 47 patients submitted to surgery. Comparisons between the "corrected" figures for the Q-1 intervals, 2-OS intervals, and Q-1 minus 2-OS values and the size of mitral orifice found at operation have been made. Appreciable correlation was evident between valve size and both the 2-OS interval and the Q-1 minus 2-OS value. No significant correlation was observed between the Q-1 interval and valve size. Postoperative observations in 17 patients revealed shortening of the Q-1 time in 5 patients, lengthening of the 2-OS interval in 14 patients, and decrease in Q-1 minus 2-OS value in 13 patients, the changes being greater in those patients exhibiting more severe mitral stenosis. When both the 2-OS interval is less than 0.09 second and the Q-1 minus 2-OS value is greater than -1.0 the likelihood of significant mitral stenosis is great. Fewer predictive errors in valve size are made when the values observed in a single patient satisfy both indices rather than either index used alone as a criterion.

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CARDIAC PACEMAKER AND DEFIBRILLATOR WITH VARIABLE OUTPUT

Karl E. Karlson, M.D., and Marvin L. Gliedman, M.D.,** Brooklyn, N. Y.*

IT HAS BEEN demonstrated that electrical stimuli may be used to induce myocardial fibrillation, to defibrillate the myocardium, or to control the heart action. The response of the myocardium is determined by the characteristics of the stimulus. Alternating current (60 c.p.s.) of less than 28 volts will cause fibrillation (never defibrillation) and of greater than 85 volts will cause defibrillation (never fibrillation). Similarly, 0.5 amp. (60 c.p.s.) will cause fibrillation (never defibrillation) and 1.5 to 3.8 amp. will cause defibrillation (never fibrillation).[1] Further studies have shown that higher voltages (270) are more effective for defibrillation[2] and that short impulses are less likely to result in myocardial damage.[3] However, the optimum voltage-time relationships have not been precisely established and may vary.

The optimum stimulus for control of heart action has been more accurately determined. A pacemaker pulse may be monophasic or biphasic but should be single with a sharp rise and exponential decay. The optimum duration of pulse is 0.02 to 4 milliseconds. Voltage requirement to initiate systole is usually 2 to 3 volts (less than 20 volts).[4, 5, 6, 7] Repetitive stimulation within physiologic range is desirable (up to 120 per minute).

For the past 4 years we have used a defibrillator and pacemaker of our own design.† This instrument is constructed to allow a large variation in output while being of comparatively simple design and relatively inexpensive.

CHARACTERISTICS OF APPARATUS

The defibrillator produces pulses of up to 300 volts at 60 cycles per second. The range of frequency of the output impulses is 0 to 400 per minute. The duration of each output impulse is continuously variable between 0 per cent and 50 per cent of the interval between the initiation of successive impulses (Fig. 1; Tables I and II). It is therefore possible to set the output to

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From the Department of Surgery, State University of New York Downstate Medical Center, Brooklyn, N. Y.

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*Associate Professor of Surgery.

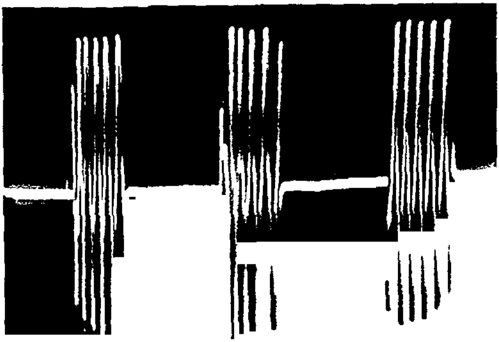
**Assistant Resident in Surgery.

†Manufactured for us by Barry Johnson, 85 Gerry Rd., Brookline, Mass.

deliver impulses of any voltage up to 300, any rate up to 400 per minute, and any desired pulse width down to one half of one cycle of the alternating current.

Pacemaker.—The output voltage of the pacemaker is continuously variable between 0 and 20 volts. The output impulses are variable between 0 and 200 per minute. Each impulse is a square wave rising sharply and decaying to 60 per cent of maximum in 3 milliseconds, one such wave being emitted per pulse (Fig. 2).

Fig 1



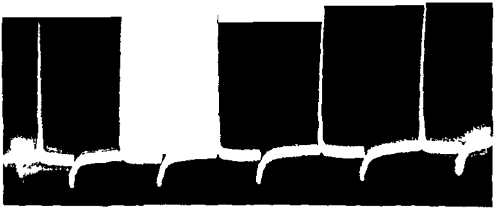


Fig. 2

Fig. 1.—Defibrillator output as seen on oscilloscope
Fig. 2.—Pacemaker output as seen on oscilloscope.

PRINCIPLES OF OPERATION

Defibrillator.—The 60-cycle input current is stepped up to 300 volts by means of a transformer (Fig. 3) and then fed to a variable autotransformer controlling the output voltage. A pair of motor-driven cam-operated switches are connected in series between the two transformers. These switches serve to open and close the circuit at the desired rate, determined by the speed of rotation of the cam that actuates the switches. The rotational velocity of the cams is controlled by a variable speed mechanism, linking the cam-shaft to the drive motor.

TABLE I. DURATION OF DEFIBRILLATOR PULSE*

FRACTION OF MINUTE

PULSE RATE DIAL SETTING	PULSE WIDTH DIAL SETTING									
	1	2	3	4	5	6	7	8	9	10
(1)†	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50
0.5 (50)	0.001	0.002	0.003	0.004	0.005	0.006	0.007	0.008	0.009	0.010
1 (100)	0.0005	0.0010	0.0015	0.0020	0.0025	0.0030	0.0035	0.0040	0.0045	0.0050
1.5 (150)	0.00032	0.00064	0.00096	0.00128	0.00160	0.00192	0.00224	0.00256	0.0288	0.00320
2 (200)	0.00025	0.0005	0.00075	0.0010	0.00125	0.00150	0.00175	0.00200	0.00225	0.00250
3 (300)	0.000165	0.00033	0.000495	0.000660	0.000825	0.000990	0.001155	0.001320	0.001485	0.001650
4 (400)	0.000125	0.000250	0.000375	0.000500	0.000625	0.000750	0.000875	0.001000	0.001125	0.001250

*Length of defibrillator output pulse at selected settings of *Pulse Width* and *Pulse Rate* dials. Any desired pulse width within this range may be obtained by setting the dials appropriately.

†( ) = pulses per minute.

TABLE II. DURATION OF DEFIBRILLATOR PULSE*

NUMBER OF CYCLES (60 C.P.S.)

PULSE RATE DIAL SETTING	PULSE WIDTH DIAL SETTING									
	1	2	3	4	5	6	7	8	9	10
(1)†	180	360	540	720	900	1080	1260	1440	1620	1800
0.5 (50)	3.6	7.2	10.8	14.4	18.0	21.6	25.2	28.8	32.4	36
1 (100)	1.8	3.6	5.4	7.2	9.0	10.8	12.6	14.4	16.2	18.0
1.5 (150)	1.2	2.4	3.6	4.8	6.0	7.2	8.4	9.6	10.8	12.0
2 (200)	0.9	1.8	2.7	3.6	4.5	5.4	6.3	7.2	8.1	9.0
3 (300)	0.6	1.2	1.8	2.4	3.0	3.6	4.2	4.8	5.4	6.0
4 (400)	0.45	0.9	1.35	1.80	2.25	2.70	3.15	3.60	4.05	4.50

*Length of defibrillator output pulse in cycles at selected settings of *Pulse Width* and *Pulse Rate* dials.

†( ) = pulses per minute.

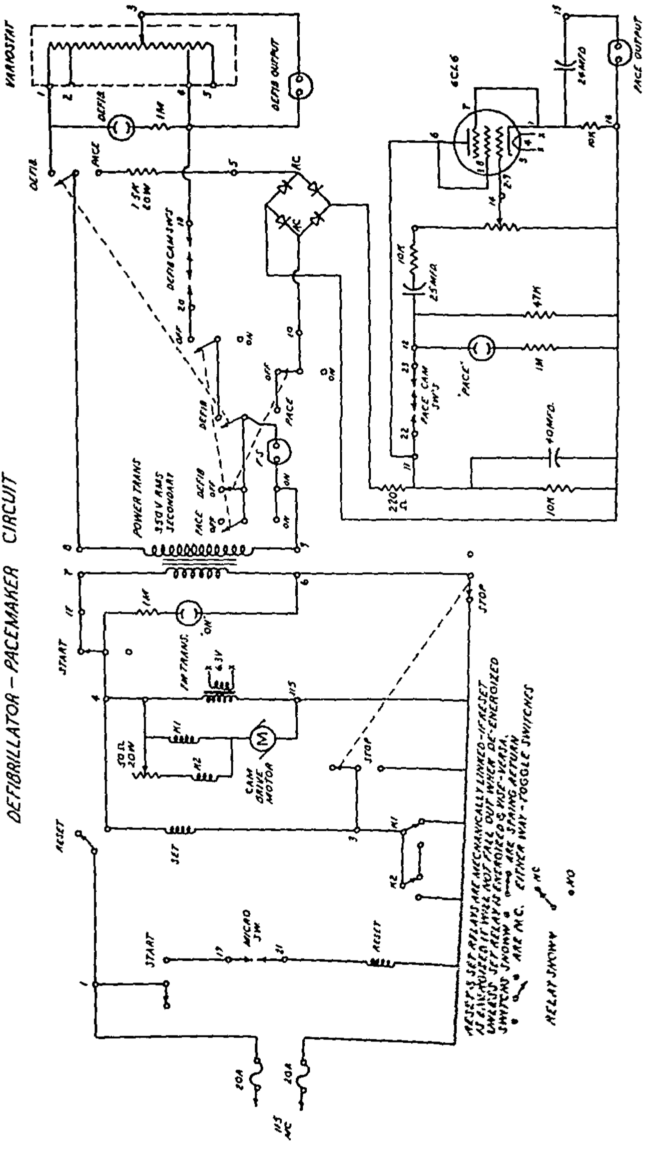

DEFIBRILLATOR – PACEMAKER CIRCUIT
VARIOSTAT
DEFIB OUTPUT
DEFIB
1M
PACE
1.5K 20W
DEFIB CAM SW'S
OFF
ON
DEFIB
PACE
PS
POWER TRANS 350 V RMS SECONDARY
PACE OFF
DEFIB OFF
6CL6
24 MFD
PACE OUTPUT
10K
.25 MFD
47K
'PACE'
1M
PACE CAM SW'S
40 MFD
220 Ω
10K
START
'ON'
1M
FIL TRANS. 6.3V
115
50 Ω 20W
K1
K2
CAM DRIVE MOTOR
STOP
RESET
SET
START
MICRO SW
RESET
20A
20A
115 A/C
RESET & SET RELAYS ARE MECHANICALLY LINKED-IF RESET IS ENERGIZED IT WILL NOT FALL OUT WHEN DE-ENERGIZED UNLESS SET RELAY IS ENERGIZED & VICE-VERSA. SWITCHES SHOWN ARE SPRING RETURN ARE N.C. EITHER WAY-TOGGLE SWITCHES
RELAY SHOWN NC NO

Fig. 3.—Wiring diagram of defibrillator-pacemaker.

The duration of the output impulse is controlled by rotating one of the switches with respect to the other on the common cam-shaft. When the switches are actuated simultaneously, the output is maximum (50 per cent of interval between onset of successive impulses). When one lags the other, the impulse width is diminished as the lag increases, to the point where one switch opens at the same time the other closes, making the impulse width 0.

Pacemaker.—The source of the pacemaker output impulse is a DC power supply. The DC voltage is switched on and off by a single cam-actuated switch. The rotation of this cam is controlled by a variable speed mechanism linking the cam-shaft and the drive motor. The resulting output impulse is a sharp square wave of constant duration which is fed into a differentiating circuit in order to obtain pulses that rise sharply and decay exponentially within 3 milliseconds.

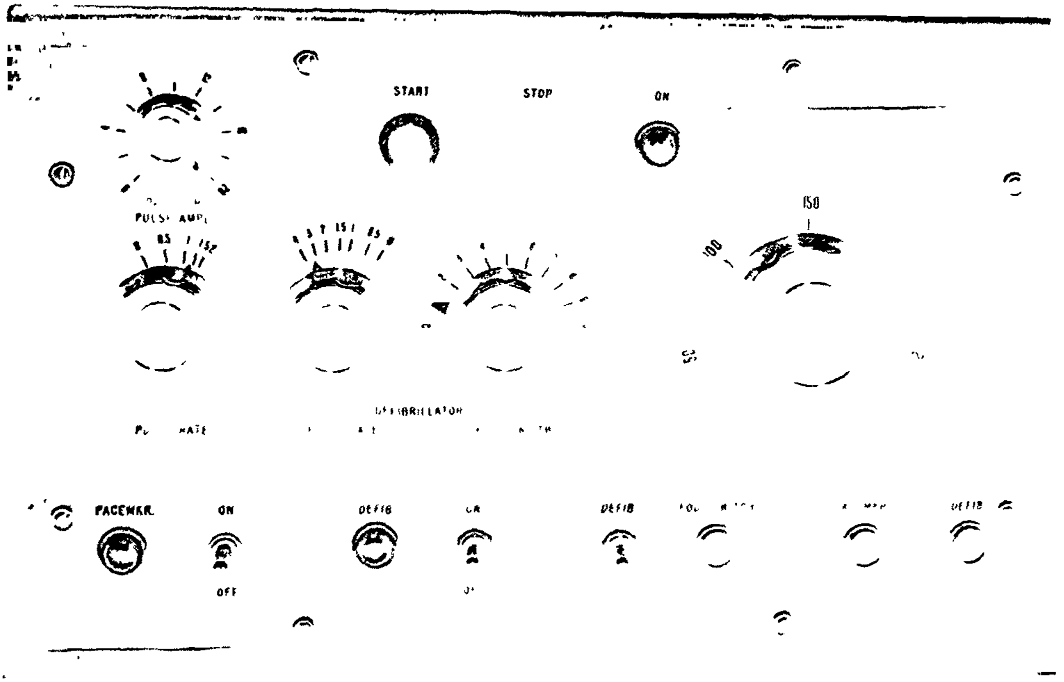


Fig. 4.—Control panel of unit.

OPERATION

Defibrillator.—The voltage is varied by the front panel control labeled *Defib. Pulse Ampl.* (defibrillator pulse amplitude) (Fig. 4), which is calibrated from 0 to 300. The pulse repetition rate is varied by the control labeled *Defibrillator Pulse Rate,* calibrated from 0 to 4, and indicating rate in hundreds of pulses per minute (0-400). The length of the output impulse is determined by the setting of the *Defibrillator Pulse Width* control. This control is calibrated from 0 to 10 which indicates 0 to 50 per cent of the pulse interval as the duration of the output impulse. The defibrillator electrodes are attached at the

Defib Output (defibrillator output) connector The defibrillator *On Off* switch, which has a spring return to the *Off* position, may be used to energize the defibrillator circuit (rather than using the foot switch) The *Defib Pacemkr* (defibrillator pacemaker) selector switch must be in the "defibrillator" position The *Defib* (defibrillator) lamp flashes synchronously with each defibrillator impulse and indicates the rate and duration of each impulse

Pacemaker —Output voltage is controlled by the *Pacemkr Pulse Ampl* (pacemaker pulse amplitude), calibrated from 0 to 20 (volts) The *Pacemkr Pulse Rate* (pacemaker pulse rate) controls the rate of pacemaker pulses and is calibrated from 0 to 2, indicating the pulse repetition rate in hundreds of pulses per minute The pacemaker electrode is connected to the *Pacemkr Output* (pacemaker output) The pacemaker circuit is energized by switching the pacemaker *On Off* switch to the *On* position The *Defib Pacemkr* (defibrillator pacemaker) selector switch must be in the *Pacemkr* (pacemaker) position Each pacemaker pulse is indicated on the *Pacemkr* lamp

To turn the unit on preparatory to use, both the defibrillator and pacemaker pulse rate controls must be turned to 0 because the 0 stop is interlocked with the motor starting circuit With these controls at 0, the start button is depressed for about 2 seconds and then released The *On* lamp then lights There is also a stop button to de energize the unit

Comment —This instrument provides continuous variability of voltage, pulse width, and pulse frequency within known ranges of effectiveness for defibrillation Optimal pulse characteristics may easily be obtained Wide variability is available for experimentation The pacemaker component utilizes pulse characteristics previously determined to be satisfactory and the pulse frequency is variable within a range suitable for all clinical and most experimental applications

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TRACHEAL COMPRESSION CAUSED BY AN ANOMALOUS INNOMINATE ARTERY ARISING FROM A BRACHIOCEPHALIC TRUNK

Charles Fineberg, M.D., and Henry C. Stofman, M.D., Philadelphia, Pa.

VASCULAR ANOMALIES of the superior mediastinum are surgically important because they may produce compression of the trachea and of the esophagus.[1, 2, 3] Anterior compression of the trachea without involvement of the esophagus may occur. It may be produced by mediastinal tumor, anomalous innominate artery, anomalous left carotid artery, and incomplete development of the tracheal cartilages. Gross[4] states that the left carotid artery may have a common origin with an anomalous innominate artery; this origin is from the distal portion of the arch of the aorta. Anterior compression of the trachea usually results in dyspnea, cyanosis, inspiratory and expiratory crowing, and recurrent pneumonitis because of inability to raise secretions.

The subject of this report is a case of anterior tracheal compression caused by an innominate artery originating from a brachiocephalic trunk. A review of the literature fails to reveal such a congenital anomaly causing tracheal compression.

CASE REPORT

An 8-month-old Negro female was admitted to the pediatric ward on Aug. 26, 1957, with a 2-month history of respiratory difficulty. The prenatal history was noncontributory. The child was a product of a normal delivery and weighed 6½ pounds at birth. She was in relatively good health for 2 months when she experienced an attack of chicken pox from which she recovered without difficulty. At the age of 2 months respiratory difficulty occurred, characterized by a definite expiratory wheeze and tugging respiration which were exacerbated on exertion and crying. The child did not cough and was able to eat well. Swallowing liquids at times was followed by severe cyanosis. On three occasions in the following 6 months the child experienced acute respiratory distress and cyanosis, which required hospitalization for periods of 2 to 3 weeks. X-ray studies at that time in another hospital were reported as being within normal limits. Following the third period of respiratory difficulty the child was seen in the outpatient department of the Jefferson Hospital and x-ray studies of the chest with barium swallow were performed. Lateral chest roentgenograms showed anterior tracheal compression just below the thoracic inlet.

Physical examination on admission to the hospital revealed a well-developed 8-month-old Negro female who was lying in the prone position with the head extended markedly on the trunk. The child was in obvious respiratory distress and a gross expiratory wheeze was

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From the Department of Surgery, Jefferson Medical College Hospital, Philadelphia, Pa.

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present. Her temperature was 37.5° C., pulse 130, and repirations 40 per minute. Positive physical findings were confined to the thorax. Many coarse rhonchi were heard in the upper portion of the thorax and thought to be transmitted to the upper tracheobronchial tree. An expiratory stridor was present. Laboratory findings were as follows: hematocrit 32, hemoglobin 7.8 Gm. per 100 ml., white blood cell count 6,000, segmented neutrophils 36, lymphocytes 62, and monocytes 2. Urinalysis was within normal limits. Culture of the nose and throat revealed normal flora and bronchial cultures revealed an occasional staphylococcus. The serology was reported as negative. The injection of purified protein derivative, strengths No. 1 and No. 2, produced a negative response. Electrocardiogram revealed sinus tachycardia with no evidence of heart disease. X ray studies of the chest showed a prominent thymic shadow. In the lateral views there was narrowing of the lumen of the trachea along its anterior margin just below the thoracic inlet (Fig. 1).

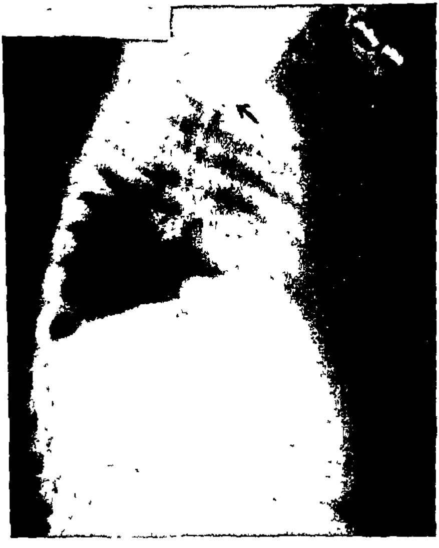

Fig 1

Bronchoscopy performed on Sept. 9, 1957, revealed constriction of the trachea just below the cricoid cartilage and this was thought to be due to extrinsic compression. The attending staff considered the pathologic condition to be due to an anterior mediastinal mass compressing the trachea.

On consultation, the surgeons considered the constriction of the trachea at the level of the thoracic inlet to be due to an anomalous vessel, either an anomalous innominate, or left carotid, artery. No roentgenologic evidence of mediastinal mass could be found. Surgical exploration and correction of the anomaly was recommended.

Exploratory thoracotomy through a left anterolateral incision was performed on Sept. 16, 1957, under endotracheal anesthesia. A small endotracheal tube was passed without difficulty. After dissection of the mediastinum it became apparent that we were dealing with a brachiocephalic vessel which originated from the distal aspect of the aortic arch. This common trunk gave off the innominate artery and the left common carotid artery 2.2

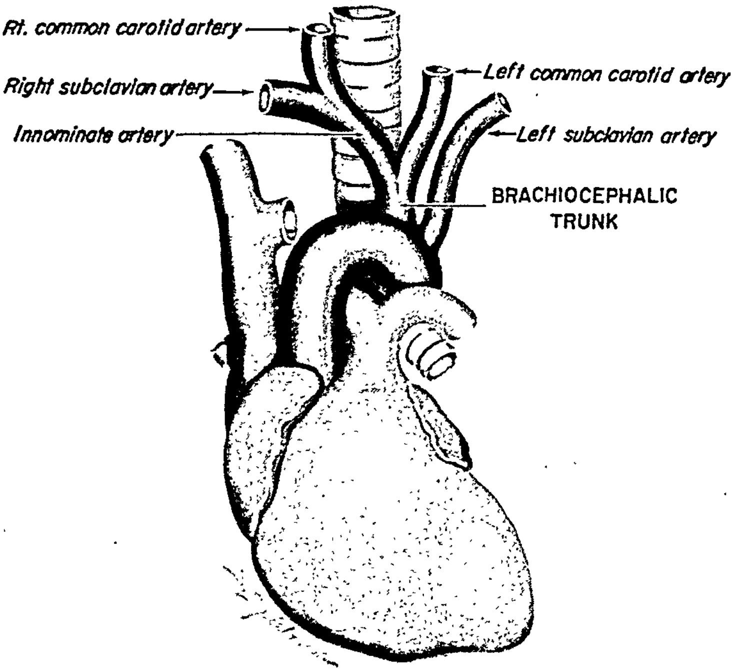
Rt. common carotid artery
Right subclavian artery
Innominate artery
Left common carotid artery
Left subclavian artery
BRACHIOCEPHALIC TRUNK

Fig. 2.

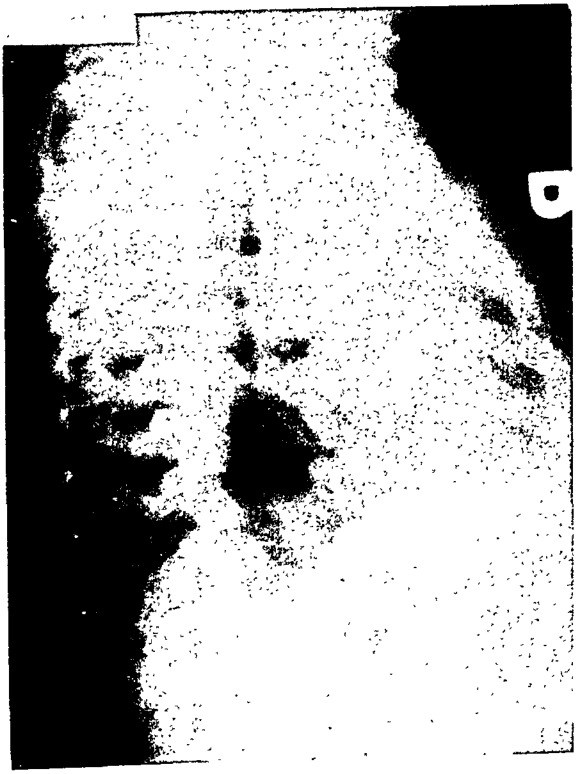

Fig. 3.

cm from its origin on the aortic arch The left subclavian originated approximately 0 5 cm to the left of the brachiocephalic vessel (Fig 2) The innominate artery followed a 45 degree course through the anterior mediastinum and passed anterior to the trachea just below the thoracic inlet The entire brachiocephalic trunk, the innominate and carotid arteries were completely freed by sharp dissection Three sutures were placed throughout the adventitia of the brachiocephalic trunk at its origin from the aorta Two silk sutures were placed through the adventitia of the innominate artery as it crossed over the trachea All these sutures were brought out through the sternum This procedure pulled the anomalous innominate artery off the trachea and held it in satisfactory position

The thorax was closed without drainage The procedure was tolerated well and the patient was returned to the recovery room in good condition After recovery from anesthesia the child's respirations were obviously markedly improved The respiratory stridor was no longer evident The postoperative course was complicated by a rectal temperature elevation to 38 8° C on the second postoperative day Roentgenograms taken at this time showed atelectasis of the right upper lobe A high humidity oxygen tent was utilized The temperature returned to normal levels on the third day and the rest of the postoperative period was completely uncomplicated

The patient was discharged on the twelfth postoperative day and was last seen 6 months after operation at which time the mother stated that the previous respiratory difficulty had been completely relieved The child was entirely normal and showed satisfactory growth and development Follow up x rays revealed complete relief of the tracheal obstruction (Fig 3)

DISCUSSION

Anterior compression of the trachea, causing respiratory obstruction without involvement of the esophagus may be caused by one of two vascular anomalies An anomalous innominate artery may originate farther to the left on the aortic arch and pass anterior to the trachea in its course to the right thorax Depending on its length and laxity, it may or may not cause enough narrowing of the trachea to produce respiratory obstruction

An anomalous left common carotid artery originates from the right side of the aortic arch and also passes anterior to the trachea It can cause obstruction in the same manner as an anomalous innominate artery

The symptoms caused by these anomalies are referable to the respiratory tract Symptoms of esophageal obstruction such as occur with double aortic arch and right aortic arch with a ligamentum arteriosum are absent, as the esophagus is not impinged upon Recurrent, pulmonary infection, dyspnea, cyanosis, crowing respiration and suprasternal tugging may be seen with this type of tracheal obstruction The patient may assume a characteristic position, a prone position with hyperextension of the neck seems to improve expiratory exchange Flexion of the head on the trunk exacerbates respiratory distress

Lateral roentgenograms of the chest will reveal anterior narrowing of the tracheal air column at its lower third Tracheograms performed with opaque media will more clearly delineate the site of compression Tracheograms were not performed on our patient, since the site of compression was readily detected on regular lateral chest films Angiocardiography or retrograde aortography may be of great value in the rare case, but is thought to be usually an unnecessary diagnostic procedure

Endoscopy may be helpful in viewing the site and determining the cause of the tracheal compression At times, tracheal compression due anomalies may cause transmitted pulsations which are readily visible through the bronchoscope. Compression due to incomplete development of the tracheal cartilages can be determined by endoscopic examination as the caliber of the tracheal lumen will decrease on expiration.

Anterior compression of the trachea may also be caused by a mediastinal mass. Lateral x-ray views of the chest should then reveal an anterior opacity impinging on the trachea.

EMBRYOLOGY

The formation of a brachiocephalic trunk in the human being has not been explained. The brachiocephalic trunk presents as a part of the adult circulation in the sheep and dog.

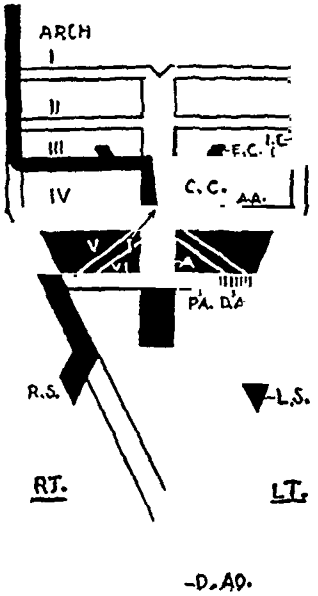

Fig. 4.—Coarctation of the aorta showing diagrammatic sketch of the aortic arches. *Blocked areas represent the definitive arteries, unblocked areas those that disappear.*

I, II, III, IV, V, and *VI* are the arches. *E. C.*—External carotid. *C. C.*—Common carotid. *I.*—Innominate. *A. A.*—Aortic arch. *A.*—Aortic sac. *P. A.*—Pulmonary artery. *D. A.*—Ductus arteriosus. *R. S.*—Right subclavian. *L. S.*—Left subclavian. *D. Ao.*—Descending aorta. (*From* Herbut: Surgical Pathology, ed. 2, Philadelphia, 1954, Lea & Febiger.)

In the human being, the aortic sac, its left horn, and the left fourth arch artery form the arch of the definitive aorta (Fig. 4). The right horn of the aortic sac elongates to become the innominate artery. The proximal part of the left third arch artery becomes the left common carotid artery.[5]

We postulate that the failure of formation of cleft in the aortic sac labeled *A* in the diagram (Fig. 4) would cause the development of a common trunk between the innominate artery labeled I and the left carotid artery labeled *C. C.* The pull of the left common carotid at its origin from the trunk might also explain the position of the brachiocephalic trunk on the left of the midline.

SUMMARY

1 A patient with anterior tracheal compression by an anomalous innominate artery originating from a brachiocephalic trunk is reported

2 The surgical correction of the anomaly is detailed

3 A possible explanation of the embryologic development of this anomaly is suggested

The authors wish to thank Peter A Herbut, M D, Professor of Pathology of the Jefferson Medical College, for permission to use Fig 4 in this article and for his advice on the developmental anatomy of this anomaly

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TRAUMATIC RUPTURE OF THE ESOPHAGUS

Robert E. Nelson, M.D., M.S., Sioux Falls, S. D.

SINCE Barrett's[1] description of the successful repair of a postemetic perforation of the esophagus in 1946, at least 200 cases have been reported, describing the primary surgical attack, and successful repair of the lesion. Mechanism of rupture has evoked considerable discussion and the advancement of many theories. Many anatomic and physiologic studies have been performed on the esophagus in an attempt to prove the method of perforation. It has been noted that perforation almost invariably occurs in the left lateral posterior aspect of the esophagus, several centimeters above the hiatus. Mackler,[2] in a study of 65 autopsy specimens, ligated the cardia of the stomach and the proximal portion of the esophagus. He then distended the specimens with air and noted that the esophagus perforated in a longitudinal direction in the left lateral posterior position, in all but 3 cases. Mosher[3] has described the anatomic features of the lower esophagus which probably contribute to rupture in this area. He noted that the circular smooth muscle of the lower esophagus becomes longitudinal close to its junction with the stomach and fans out over the stomach to help form the muscular layers. The longitudinal direction of the fibers allows easy separation, so that the mucosa, which is unsupported with a submucosal layer, can herniate through and burst. Mackler, in his study, noted that muscle fibers split first, the mucosa then bulges through the separation and ruptures, thus explaining the longitudinal character of ruptures in this area. The basic theory of mechanism, which appears most reasonable, is that the forceful ejection of gastric contents into the anatomically weak lower esophagus, during the process of vomiting, distends the lower esophagus to the point of rupture. A case report of an individual, who was struck in the epigastrium immediately after a meal with a resulting rupture of the lower esophagus, is presented because it appears to lend credence to the theory that rupture is caused by a transmission of force from the stomach into the lower esophagus, via the suddenly ejected gastric contents.

CASE REPORT

A 46-year-old rancher (H.H.) was admitted to the hospital with a history of having been crushed between two trucks, immediately following a hearty breakfast. The patient

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The patient's postoperative course was relatively uneventful. Three hundred cubic centimeters of serosanguineous fluid was aspirated from the right thorax. On the fifth day the temperature was normal. On the seventh day, the Levin tube was removed and the patient was started on a clear liquid diet. On the tenth day, the patient was advanced to a full liquid diet which, by the fourteenth day, was changed to a soft diet. The chest tube was removed on the fourteenth day. Since this time, the patient has returned to his work and has had no further complaints.

DISCUSSION

A review of the literature reveals 6 cases[2, 4-8] of rupture of the lower esophagus, following nonpenetrating trauma to the epigastrium and lower chest. Five cases died without a diagnosis, the sixth[8] survived with closed drainage. It is believed that the forceful ejection of the patient's breakfast from his mouth immediately upon being struck by the truck is significant since it demonstrates the rapid emptying of gastric contents into the esophagus. Most cases of postemetic rupture of the esophagus occur when the patient vomits following ingestion of a large meal, or a heavy drinking bout. Because the rupture in the above case was identical with the type known as postemetic perforation, one may assume that similar etiological factors are present in the two groups of cases. Both have in common the forceful ejection of gastric contents into the anatomically weak lower esophagus. The lack of survivors following indirect trauma denotes a general unawareness of this type of chest injury. Early definitive treatment gives good results, as evidenced by the large number of successfully repaired postemetic esophageal ruptures. An awareness of the possibility of esophageal perforation from nonpenetrating injury will certainly lead to the early discovery of the lesion, since diagnosis is easily accomplished by simple radiologic procedures.

SUMMARY

A case of rupture of esophagus due to a blow upon the stomach is reported (1) because of the light it throws on postemetic rupture of the esophagus, and (2) because of its successful treatment by primary repair.

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The patient's postoperative course was relatively uneventful. Three hundred cubic centimeters of serosanguineous fluid was aspirated from the right thorax. On the fifth day the temperature was normal. On the seventh day, the Levin tube was removed and the patient was started on a clear liquid diet. On the tenth day, the patient was advanced to a full liquid diet which, by the fourteenth day, was changed to a soft diet. The chest tube was removed on the fourteenth day. Since this time, the patient has returned to his work and has had no further complaints.

DISCUSSION

A review of the literature reveals 6 cases[2, 4-8] of rupture of the lower esophagus, following nonpenetrating trauma to the epigastrium and lower chest. Five cases died without a diagnosis, the sixth[8] survived with closed drainage. It is believed that the forceful ejection of the patient's breakfast from his mouth immediately upon being struck by the truck is significant since it demonstrates the rapid emptying of gastric contents into the esophagus. Most cases of postemetic rupture of the esophagus occur when the patient vomits following ingestion of a large meal, or a heavy drinking bout. Because the rupture in the above case was identical with the type known as postemetic perforation, one may assume that similar etiological factors are present in the two groups of cases. Both have in common the forceful ejection of gastric contents into the anatomically weak lower esophagus. The lack of survivors following indirect trauma denotes a general unawareness of this type of chest injury. Early definitive treatment gives good results, as evidenced by the large number of successfully repaired postemetic esophageal ruptures. An awareness of the possibility of esophageal perforation from nonpenetrating injury will certainly lead to the early discovery of the lesion, since diagnosis is easily accomplished by simple radiologic procedures.

SUMMARY

A case of rupture of esophagus due to a blow upon the stomach is reported (1) because of the light it throws on postemetic rupture of the esophagus, and (2) because of its successful treatment by primary repair.

Both types of rupture have in common the sudden forceful ejection of gastric contents into the anatomically weak lower esophagus.

Early diagnosis by roentgenologic studies is mandatory.

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EXPERIMENTAL USE OF NYLON MESH FOR ESOPHAGEAL SUPPORT

Thomas C. Moore, M.D., and Gustavo Bounous, M.D., Indianapolis, Ind.

THE SUCCESSFUL clinical use of fine mesh nylon for support of a markedly weakened segment of esophageal wall and for the satisfactory function of this repair, for 3 years following operation, has prompted this investigation relative to the suitability of fine mesh nylon for esophageal support.[10]

The usefulness of fine mesh nylon in providing needed support for anatomically weakened structures in various parts of the body, both experimentally and clinically, is well recorded in medical literature. The clinical utilization of nylon mesh in the repair of abdominal wall hernia defects was first suggested and carried out by Acquaviva and Bourret[1, 2] in 1944. Since that time, a number of clinicians have reported the successful use of nylon mesh in hernia repair.[4, 5, 7, 13, 15, 16, 17] Testa,[20] in 1951, was the first to study the suitability of nylon mesh in the repair of experimentally created defects in animals. He employed a wide-mesh monofilament nylon with success in the repair of musculofascial abdominal wall defects in rabbits. The senior author and Siderys,[11] in 1955, used fine-mesh nylon experimentally to repair large abdominal wall defects in dogs. Satisfactory repairs were obtained and the nylon mesh was found to be tolerated well, both on gross and microscopic examination.

Nylon mesh had been employed with success in obtaining anatomic support in other areas. Vargas and Deterling[21] have described the use of nylon net in the external support of blood vessel grafts and aneurysms. The use of nylon mesh in the repair of diaphragmatic hernias has been reported by Adler and Firme.[3] Porell and Parsons[14] have recently recorded the successful use of nylon mesh in 2 cases in the repair of troublesome perineal hernias which developed as late sequelae of pelvic exenteration.

Although impervious synthetic tubes have been employed both experimentally and clinically for esophageal replacement, the authors have been unable to discover any published experience with the use of fine-mesh nylon for esophageal support. For this reason it has seemed desirable to record our experience with the use of fine-mesh nylon in the repair and support of partially resected segments of the wall of the esophagus.

From the Department of Surgery, Indiana University Medical Center, Indianapolis, Ind.

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MATERIAL AND METHODS

Healthy mongrel dogs were used. A mixture of oxygen and ether, delivered through an endothracheal tube by means of a mechanical respirator, was employed for anesthesia following induction with intravenous Pentothal. A left sixth intercostal space thoracotomy incision was employed.

When the left chest was opened, the lower third of the esophagus was dissected free from surrounding structures. Straight Potts coarctation clamps were used to cross-clamp the upper and lower portions of the freed-up segment of esophagus. The Potts clamps prevented bleeding from the esophageal musculature during its extramucosal resection and greatly facilitated the dissection by providing a bloodless field. They also made easier the exposure and manipulation of this segment of esophagus. Esophageal injury did not appear to have resulted from the use of these clamps in any of the animals studied.

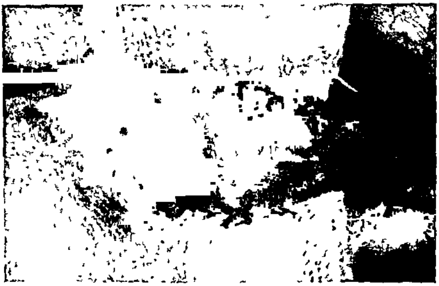

Fig. 1—Photograph of the esophagus, at the time of operation, showing the appearance of the fine-mesh nylon patch immediately after its placement.

With an area of esophagus secured between Potts coarctation clamps, an oval segment of esophageal musculature was resected. The denuded areas of esophagus averaged 2.5 by 3.5 cm. in size. It soon became apparent that relatively little weakness in the wall of the lower esophagus of the dog was produced by an extramucosal resection of muscle in this area. The mucosa and submucosa of the lower portion of the canine esophagus are rather thick and possess a surprising degree of strength. The defect which had been created in the wall of the esophagus was repaired by suturing in place, with some slight overlap, a patch of sterile nylon mesh (241-F).* The nylon mesh contained 270 by 204 threads per square inch. Interrupted sutures of 4-0 or 5-0 silk were employed (Fig. 1). The Potts clamps were released when the nylon mesh patch was secured.

The chest wall was closed in layers and a catheter which was left in the chest during the closure was aspirated and withdrawn. Esophageal defects were created and repaired with fine-mesh nylon patches in this manner in 11 dogs. In 4 additional dogs, defects were created, but were left unrepaired, to serve as controls.

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*The nylon was obtained from Stehli Company, Inc., 1372 Broadway, New York, N. Y.

RESULTS

All 4 of the control dogs were sacrificed between 3 and 4 months following operation. There was no evidence in any of the animals of bulging or distortion of the esophagus or of ischemic or necrotic change in the area of muscle resection. Weakness of the esophageal wall in the area of the muscle defect could not be demonstrated by distention of the esophagus with water under pressure. From these observations, it was apparent that significant esophageal weakness could not be produced by extramucosal resection of the esophageal musculature in the dog. It was also of interest that rather extensive resection of the musculature could be carried out without the development of ischemia or other disturbances in the underlying structures.

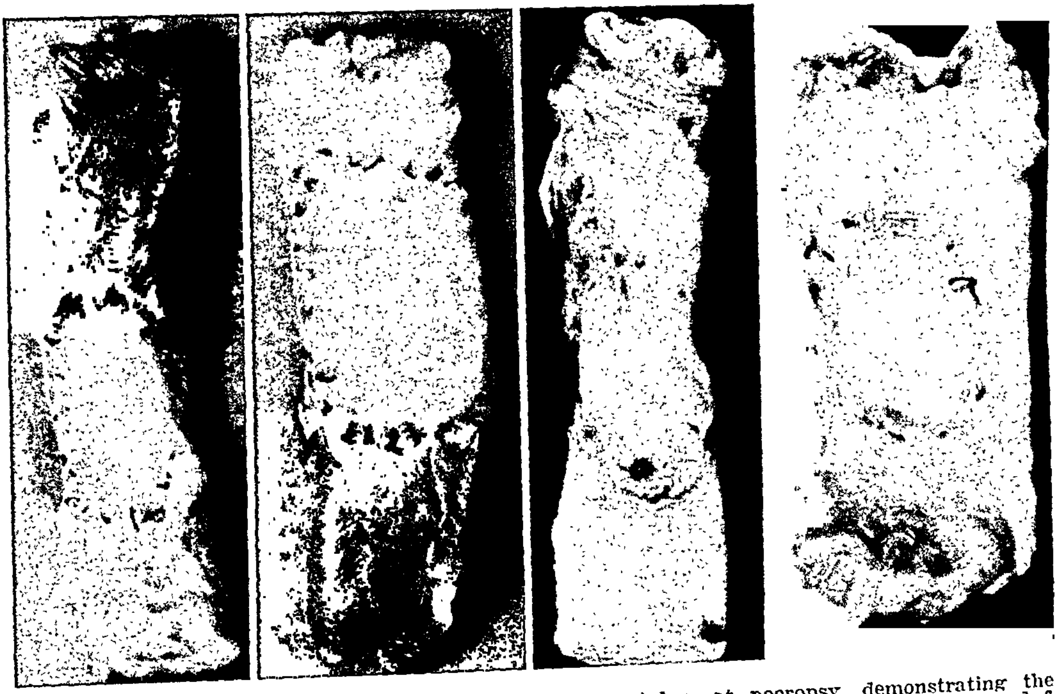

Fig. 2.—Photograph of segments of esophagus, taken at necropsy, demonstrating the satisfactory tissue tolerance and retention of shape and position of the nylon patch 5 and 6 months after operation.

The fine-mesh nylon appeared to be tolerated quite well in all 11 animals in which it was used to replace resected esophageal musculature (Fig. 2). Post-mortem studies of the segment of esophagus containing the nylon mesh patch were carried out 1 month following operation in 2 animals and 4 months following operation in 1 animal. Eight of the animals were sacrificed between 5 and 6 months after operation. No areas of esophageal weakness could be demonstrated at autopsy and no bulging could be demonstrated in the "supported" area by distending the excised segment of esophagus with water under pressure. A remarkable absence of gross reaction in the surrounding tissue to the presence of the nylon patch was observed. In all

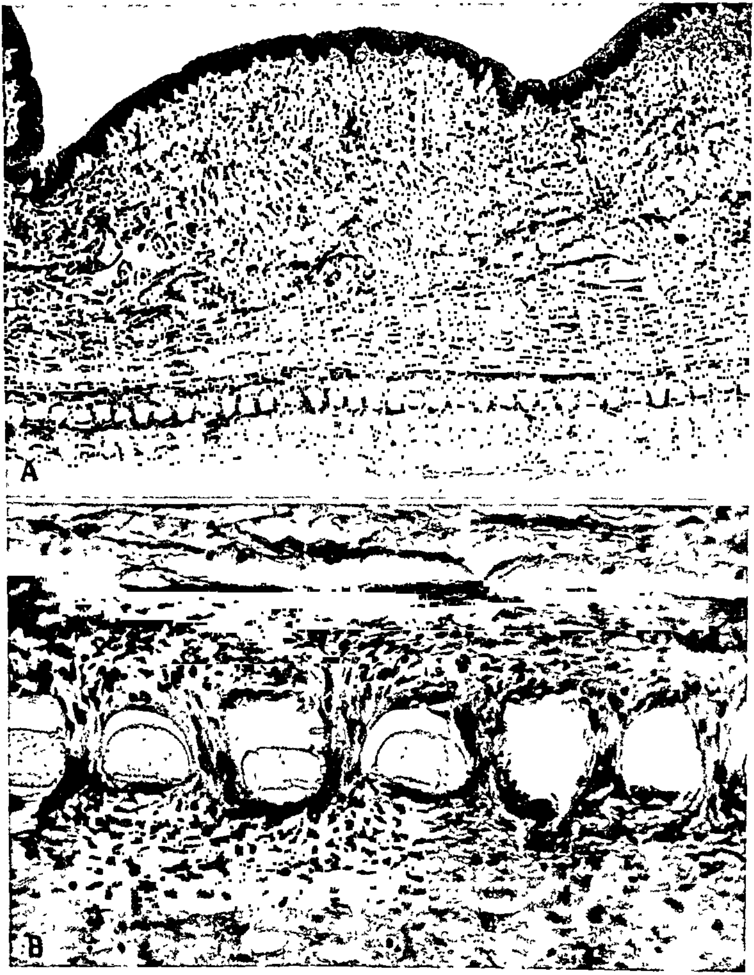

Fig. 3.—Photomicrographs, under high and low power, illustrating the excellent manner in which the nylon mesh was tolerated and incorporated into the structure of the wall of the esophagus 5 months following operation.

of the animals, the nylon patch and all of its securing interrupted silk sutures had remained intact and in place. There was no evidence of fluid accumulation, encystment, or infection in any of the animals. A minimal degree of transverse wrinkling of the fine-mesh nylon was encountered in 1 of the animals. There was no wrinkling of the nylon patch in the 10 remaining dogs. Neither scarring nor constriction of the esophagus were noted at the site of graft placement in any of the animals. The esophageal mucosa in the areas supported by the fine-mesh nylon graft was normal in all of the animals.

Microscopic study of the areas of nylon replacement of esophageal musculature revealed excellent tolerance of the nylon patch (Fig. 3). Virtually no reaction in the tissue surrounding the foreign body was encountered. The nylon patch in all of the animals appeared to be firmly incorporated into the surrounding tissue through the invasion of its interstices with fibroblasts. There was no evidence of gross or microscopic damage which might have resulted from the use of the Potts coarctation clamps for hemostasis and manipulation of the esophagus during operation.

DISCUSSION

From a review of the literature, it is apparent that little harm can come from leaving a small area of submucosa bare of muscular covering. Small areas of mucosa are frequently and successfully left bare intentionally in other portions of the alimentary tract, especially in performing cardiac and pyloric myotomies at the extremities of the stomach. In the dog with its thicker and more substantial esophageal mucosa, even larger areas of submucosa, as this study would seem to indicate, may be left barren of muscular covering and support with safety.

The principal published clinical experience with extramucosal resection of segments of the wall of the thoracic esophagus concerns the surgical management of benign tumors of the esophagus, mainly leiomyomas.[6, 8, 18, 19] In most cases, the defect following removal of a leiomyoma has been repaired successfully by approximating the adjacent esophageal muscle over the defect. Occasionally the remaining mucosa is quite thin and further steps may be required to prevent its subsequent destruction. In 2 of the 11 cases reported by Harrington,[8] extremely thin areas of remaining mucosa were incised and the remaining mucosa was closed with the reconstruction of the outer wall of the esophagus. However, when larger extramucosal defects occur it is apparent that such means cannot be resorted to without accepting the risk of significantly narrowing the lumen of the esophagus. It is also desirable to avoid entering the esophageal lumen whenever possible. Mucosal difficulty has been reported following extramucosal resection of benign esophageal tumors. Meade,[9] in discussing the paper of Sweet and his associates,[19] reported that one of two extramucosal resections was complicated by disintegration of the mucosa and the death of the patient. It is possible that other difficulties may have occurred, but have escaped publication.

Benign esophageal tumors, on occasion, may completely encircle the esophagus and may involve a rather considerable length of this structure. Nissen,[12] in 1949, reported the extramucosal removal of a large, circumferential leiomyoma from 10 cm. of the esophagus. The rather lengthy segment of barren mucosa was wrapped in a pedicle flap of lung tissue and the patient survived. Other measures, such as the use of pleural flaps, have been reported for the support of weakened areas of esophagus.

Although significant weaknesses in the esophagus wall could not be produced by the techniques of extramucosal resection employed in this study, as illustrated by the experience with the control animals, the ability of nylon mesh to support areas of anatomic weakness in the human body is well established. It may be assumed that this ability would be as effective in supporting esophageal weaknesses as those occurring elsewhere. One of the more important facets of this study was the demonstration of the tolerance of the esophagus for the nylon mesh and the capacity of the nylon mesh to remain intact and in place, despite the movement and changes in size to which the esophagus is subjected during deglutition. The nylon mesh was tolerated well in the wall of the esophagus, both grossly and microscopically. Wrinkling seldom was encountered. There was no fibrosis or contraction of the nylon graft and neither stricture or narrowing of the esophageal lumen was encountered. The appearance of the underlying mucosa remained normal in all cases. Neither fluid accumulation, encystment, nor infection occurred.

The cross-clamping of the esophagus above and below the area of extramucosal resection with straight Potts coarctation clamps proved to be a valuable aid in the handling of the esophagus and in permitting the dissection to be carried out in a bloodless field. This maneuver appeared to be tolerated well and was not associated with any early or late untoward effects.

SUMMARY

The suitability of nylon mesh in providing support for areas of weakened structures is well established. The use of fine-mesh nylon for the replacement of resected extramucosal segments of esophagus in [illegible] dogs is reported. The nylon mesh was tolerated quite well and remained securely attached to the margins of the artificially created defect throughout the periods of observation in all of the animals studied. There was complete freedom from scarring, encystment, and infection in all. The use of fine-mesh nylon for added esophageal support when needed is recommended.

The use of noncrushing, multitoothed Potts coarctation clamps for handling the esophagus, and permitting work upon it in a bloodless field is described.

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BRONCHOPULMONARY MONILIASIS

Treatment by Segmentectomy

John H Kennedy, M D , San Diego, Calif

BRONCHOPULMONARY moniliasis, an infection of the lungs by *Candida albicans*, has been recognized for over half a century Hurwitz and Yesner[1] reported the first successful surgical extirpation of localized bronchopulmonary moniliasis in 1947 In spite of the increasing frequency with which circumscribed pulmonary lesions of obscure origin are excised as a diagnostic and therapeutic maneuver, no other reports of successful surgical treatment of this unusual pulmonary disease have been found in the literature It is the purpose of this report to record a second successful surgical management of bronchopulmonary moniliasis

CASE REPORT

A married white man, a native of New York, 35 years of age, was admitted to Scripps Memorial Hospital, La Jolla, Calif , on Nov 14, 1956, complaining of recurrent hemoptysis for 2½ years There was no history of exposure to tuberculosis The patient was stationed in the southwestern region of the United States during the Second World War until his separation from the military service on a medical survey because of essential hypertension Five years previously, following a trip to Nevada, the patient noticed an upper respiratory infection with fever and nonproductive cough, following which a photofluorogram at a public health department facility showed infiltration in the left midlung field in which a cavity subsequently appeared Intradermal injection with purified protein derivative, U S P , 0 1 mg , and coccidioidin, 0 1 c c 1 100 dilution, produced a positive reaction Cultural examinations of serial sputa were negative for tubercle bacilli and fungi at this time The patient was observed for 9 months with a presumptive diagnosis of cavitary coccidioidomycosis without evidence of change in status

The patient had smoked forty cigarettes per day for over 10 years and noted a cough productive of approximately 3 c c of grayish white mucoid sputum each day which contained small black particles He reported dyspnea on climbing one flight of stairs

In 1953, because of recurrent hemoptysis, the patient had been hospitalized, at which time bronchoscopy and bronchography were reported to show no abnormality Over the ensuing 2½ years, the patient noticed gross hemoptysis, often lasting one day, and accompanied by some left anterior chest pain, occurring approximately once per month

The family history and occupational history were not remarkable, and the review of systems was otherwise noncontributory

Physical examination revealed a well nourished man who did not appear ill, weight 163 pounds, height 68 5 inches, temperature 98 6° F , blood pressure 150/80 mm Hg, heart

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rate 80, and respirations 20. Other than for a small crusting lesion, resembling epidermophytosis, posterior to the medial malleolus of the right ankle, the physical examination was entirely normal.

Examination of the urine revealed no abnormalities; hemoglobin was 14 grams per cent, the erythrocytes numbered 5.2 million and leukocytes 6,400 per cubic millimeter with a normal peripheral blood smear. Cultures for fungi taken of skin scrapings from the scaling lesion of the right foot showed no mycotic forms in 1 month. There were no tubercle bacilli in the sputum in cultural examination of three specimens, and three specimens of sputum of the same unusual character with small black particles in it grew pure cultures of *Candida albicans* on modified eosin-methylene blue medium after the method of Weldin (San Diego County Department of Public Health Laboratory). A complement fixation test for *Coccidioides immitis* was 3-plus in the 1:2 dilution, which was thought to be nondiagnostic. A pulmonary ventilation study was normal before and after a bronchodilator.

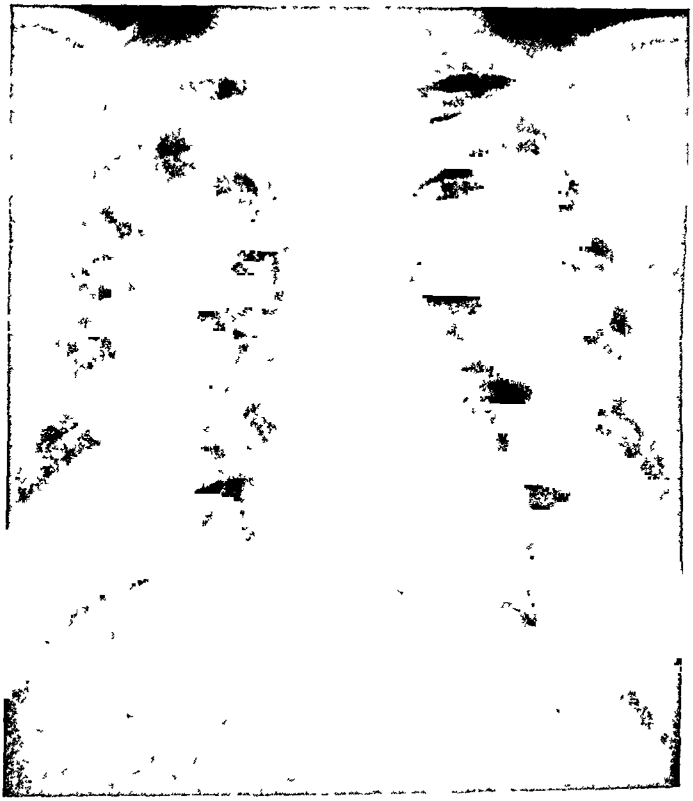

Fig. 1.—Preoperative roentgenogram of the chest. A cavity can be seen in the left mid-lung field.

In a roentgenogram of the lungs (Fig. 1), there appeared a cavity in the left mid-lung field which in the lateral view appeared to lie in the superior segment of the left lower lobe. Planograms failed to reveal calcification in the wall of the cavity and showed no other associated lesions. Preoperative bronchoscopic examination revealed no abnormality.

Surgical Procedure.—On Nov. 15, 1956, a left thoracotomy was performed through the fifth intercostal space. There was no free fluid, nor any evidence of pleural disease. At the apex of the left lung there were multiple small bullae. In the superior segment of the left lower lobe was a thin-walled cavitary lesion which could be felt through normal lung tissue, and scattered about it were a number of fibrocalcific lesions. A superior segmentectomy was carried out with ligation of the segmental vessels and interrupted suture closure of the segmental bronchus. The raw lung surfaces were closed with interrupted sutures of 4-0 silk. Anterior and posterior catheter drains were placed in the second anterior and the eighth posterior interspace and connected to water seal drainage The patient received 2,500 c c of whole blood during the procedure, and the thoracic incision was closed in layers with silk

Postoperatively, the patient's convalescence was uneventful The gross pathologic specimen is shown in Fig 2, and there can be seen a thick walled cavity measuring 3 cm in maximal diameter The wall averaged 2 to 3 mm in thickness and was firm and grayish white Microscopic examination (Thomas A Le Strange, M D) showed the above described cystic lesion to be partially lined with bronchial mucosa showing foci of squamous metaplasia Communication with a bronchiole is demonstrated in Fig 3 The majority of the cystic area was lined by fibrous tissue, into which there was a marked chronic inflammatory cellular infiltration The fibrous tissue was covered with a hemorrhagic exudate Within the cavity of the lesion, definite spore forms with mycelia were demonstrated with periodic acid Schiff stain technique These fungi were consistent with *Candida albicans* The adjacent pulmonary tissue surrounding the cystic lesion showed marked scarring, atelectasis, and chronic inflammatory changes Multinucleated cells although not numerous, were demonstrated A high power view of mycelia demonstrated with periodic acid Schiff stain technique is shown in Fig 4

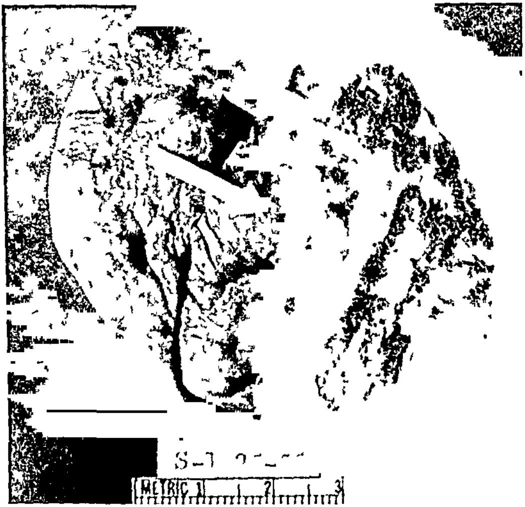

Fig 2 —The resected superior segment of the left lower lobe The arrow indicates the cavity

Four months postoperatively, although the patient felt well and had returned to work and had noted no further bleeding episodes, he noticed a return of small amounts of mucoid sputum containing small black particles Culture of the sputum was again positive for *Candida albicans* As at that time there was no other effective fungicidal agent available, the patient was treated with inhalation therapy using a bronchodilator and an aerosol of brilliant green dye in a 1 200,000 dilution by positive pressure therapy for 1 month

The patient has now been well 1 year, raises no sputum, has had no further bleeding episodes, and the small amount of mucoid secretion which the patient raises from his bronchial tree shows no cultural evidence of fungi

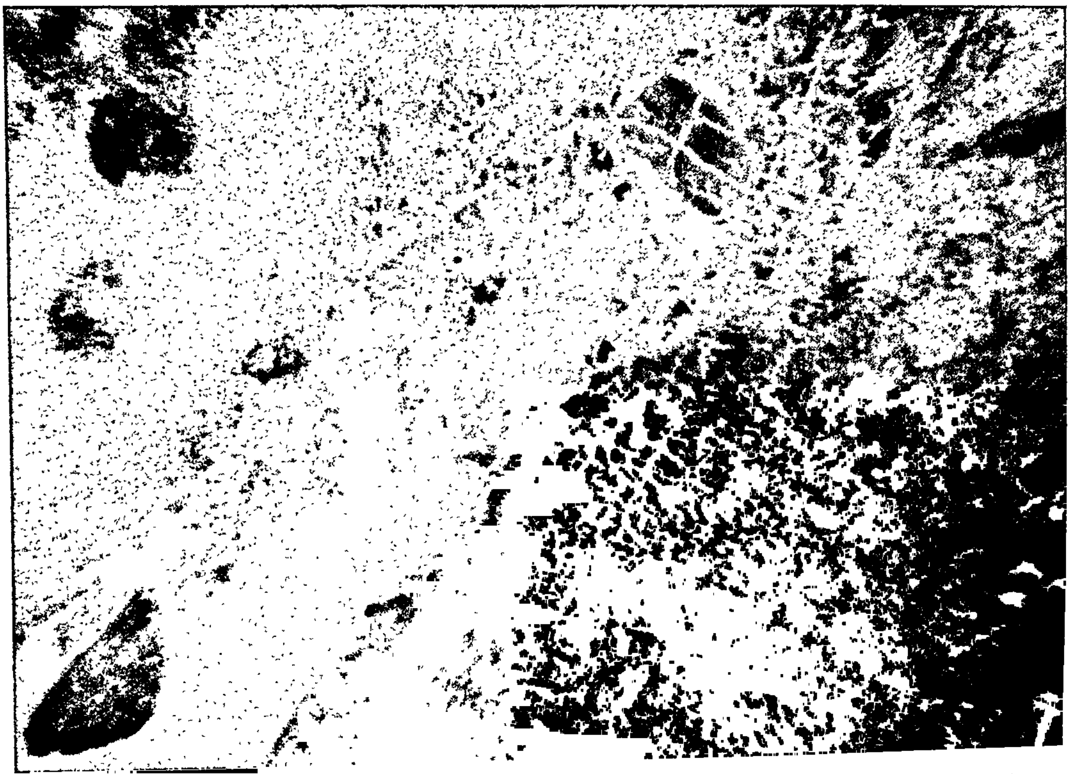

Fig. 3.—Low-power photomicrograph demonstrating communication of a cavity with a bronchiole.

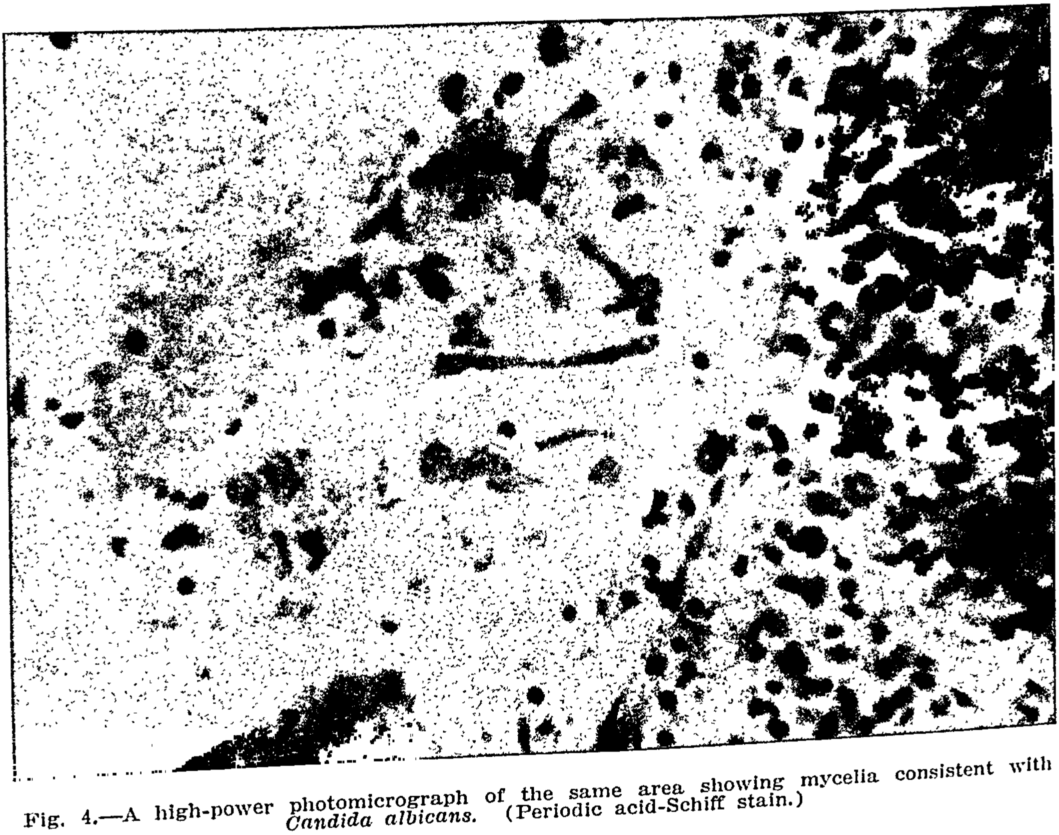

Fig. 4.—A high-power photomicrograph of the same area showing mycelia consistent with *Candida albicans.* (Periodic acid-Schiff stain.)

DISCUSSION

Pulmonary moniliasis is not as rare a disease as is generally assumed, being next in frequency to actinomycosis among the mycotic diseases of the lung[11] Although *Candida albicans* is a saprophyte present in the body in health, it has been shown to have the ability to produce an invasive and occasionally fatal pulmonary infection[2, 6, 9] The medical management of this disease has been difficult and variable Kass, Sasano, and Klein[5] reported successful treatment of one patient with brilliant green aerosol inhalation Successful treatment with brilliant green aerosol has likewise been reported by Smith and Arman,[8] in 1955 More recently Scott has reported a possible case of pulmonary moniliasis involving both lungs with dramatic response to potassium iodide therapy and has discussed the advent of a new fungicidal agent, Amphotericin B

SUMMARY

A case of symptomatic cavitary bronchopulmonary moniliasis successfully treated by segmentectomy and postoperative brilliant green aerosol therapy has been reported It is believed that this is the second reported successful surgical treatment of this disease

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SOLITARY RHABDOMYOSARCOMA OF THE PLEURA

Report of a Case With a Note on the Nomenclature of Pleural Tumors

J. T. Dubig, M.B., D. Path., Boston, Mass.

ONE of the features of striated muscle tumors is their frequent occurrence in sites in which striated muscle is either scanty or absent. This fact has led to much speculation on the tissue of origin of rhabdomyomatous tumors which arise in such places. A neoplasm illustrating this aspect of abnormal muscle cell growth is seen in the following case, which is also remarkable for the similarity of the clinical and gross pathologic findings to those found in many cases of solitary fibroblastic pleural tumor.

CASE REPORT

Clinical History.—A male retired plumber, aged 69 years at the time of his death, was first seen 3 years before this, when his main complaints were recurrent chest pain and increasing breathlessness on exertion. These symptoms had become increasingly severe since an attack of an "influenza-like" illness some 4 years before. He also maintained that he was now getting bouts of fever with shivers and he had also noticed some pain and swelling in the joints of the fingers. Physical examination revealed absent breath sounds and diminished movement over the left side of the chest and a moderate degree of hypertrophic pulmonary osteoarthropathy of the fingers and toes. A chest radiograph and subsequent fluoroscopic examination showed a large opacity with a smooth, rounded upper border in the left side of the thorax with displacement of the cardiac shadow to the right. No fluid was obtained on attempted thoracentesis and this, combined with the radiographic appearances, prompted the radiologist to suggest the diagnosis of a benign intrathoracic tumor. Bronchoscopy revealed no abnormality. Fluid aspirated from the bronchi was negative for malignant cells and numerous subsequent sputum examinations also proved negative for both malignant cells and tubercle bacilli. Clinically, he was considered to have an inoperable carcinoma of the lung and a course of palliative deep roentgen therapy was instituted. Then followed a period of 2 years, during which he had intermittent courses of this therapy to the chest lesion, with some subjective improvement after each treatment. However, as the radiographic signs appeared to be increasing while the patient's general condition remained much as before, the diagnosis of carcinoma of the lung appeared open to doubt. The radiologist felt that the appearances were still those of a tumor rather than an inflammatory lesion, but as no alternative treatment was suggested, it was decided to persist with the deep roentgen therapy.

Increasing exertional dyspnea now began to incapacitate the patient and he was readmitted to hospital, 2 years and 5 months after his initial visit. At this time, he was

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From the Laboratory of Pathology, Harvard Cancer Commission and the Cancer Research Institute, New England Deaconess Hospital, Boston, Mass.

This work was commenced in the Pathology Department, General Hospital, Brisbane, Australia.

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noted to have marked clubbing of the fingers and toes, he was dyspneic on the slightest exertion and the chest radiographs showed a total opacity of the left side of the thorax With bed rest, the patient's condition improved sufficiently for him to be discharged from the hospital, but he was readmitted 2 months later, again complaining of severe exertional dyspnea He now had dyspnea even at rest and he had noticed swelling of the feet and angles Slight cyanosis was evident and he had a mild pyrexia. A pleural biopsy was considered but dismissed because of the patient's poor general condition. Death occurred promptly. The total duration of symptoms was approximately 7 years.

Autopsy Findings—Autopsy was performed 13 hours after death. Gross hypertrophic pulmonary osteoarthopathy of the fingers and toes was noted on external examination and subsequent dissection of the involved joints confirmed this Pitting edema of the feet and ankles was present. As was anticipated, all the findings of importance were confined to the thorax. Here, there was a gross mediastinal shift to the right due to a large tumor in the left pleural cavity. This tumor measured 30 by 15 by 12 cm in its largest diameters and it lay quite free in the pleural space, the visceral and parietal pleurae being quite simply separated from the tumor mass. Several fibrous strands ran from the pleural surfaces into the tumor, these being most marked over the area of the fourth, fifth, and sixth ribs just anterior to the costovertebral junctions Adhesions were also seen over the lower portion of the neoplasm anteriorly, where fibrous strands attached it to the visceral pleura.

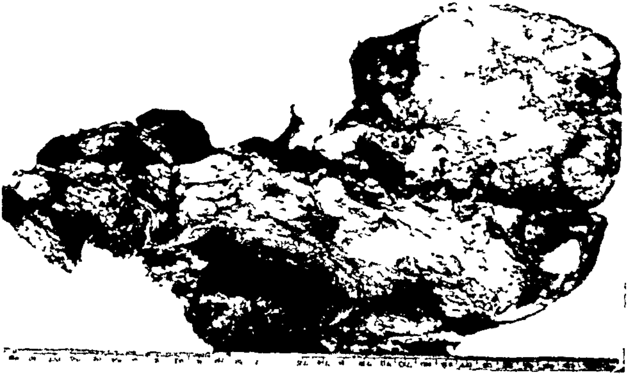

Fig 1—Cut surface of tumor Scale in centimeters

No definite point of origin of the tumor from surrounding structures could be demonstrated and no connection with the intercostal nerves or the sympathetic chain was noted. The tumor weighed 2,694 grams and appeared to be quite encapsulated, except in its superolateral portion where extensive necrotic change had taken place The capsule was smooth and glistening and showed quite distinctly the smooth lobules of underlying tumor tissue The cut surface of the tumor (Fig 1) revealed a mass composed of firm nodules of tissue which varied in color from pale pink to grayish white, some of the nodules being up to 3 cm in diameter Whorls and trabeculae of what appeared to be fibrous tissue could be seen encircling and passing through the tumor masses Numerous soft yellow areas of necrosis with occasional areas of hemorrhage were also seen and in the upper portion of the tumor this had progressed to almost complete liquefaction necrosis This was thought to be the effect of the deep roentgen therapy. At no point was any invasion of the capsule seen and no invasion of any of the underlying tissue could be demonstrated. The pleural cavity contained approximately 900 ml. of dark hemorrhagic fluid, due to the liquefaction necrosis of the upper portion of the tumor.

The underlying left lung was collapsed and the bronchi grossly infected, while the right lung also showed areas of collapse and bronchopneumonia. Dissection of the pulmonary bronchi was carried to their finest radicles but no tumors could be demonstrated. Some atherosclerosis was present in the vascular system, the liver showed evidence of passive venous congestion, and some enlargement of the prostate was seen. No other tumors were found at autopsy despite meticulous search.

Microscopic Findings.—Microscopic examination of a number of organs and tissues including the thoracic tumor was undertaken, the material being fixed in 10 per cent formol saline. Representative blocks were cut and stained by a variety of methods, those used being Mallory's phosphotungstic acid hematoxylin, Crossman's modification of Mallory's connective tissue stain, van Gieson, Masson's trichrome technique, Foot's reticulum stain, and hematoxylin and eosin. The pulmonary tissues showed areas of atelectasis with much pyogenic infection and necrosis but no areas of neoplasia. The prostate was subjected to meticulous search but benign lobular hyperplasia only could be demonstrated. The liver showed some venous congestion. The pleural tumor exhibited a quite extraordinary appearance and multiple blocks were studied, all the above-staining techniques being employed. The most striking feature was the presence of areas of large eosinophilic cells with granular cytoplasm, many of them multinucleate and showing a variety of forms (Fig. 2). Round, triangular, and elongate cells were seen, some. 40 to 50 microns in diameter, the majority having between 2 and 4 nuclei. These nuclei were generally eccentrically placed in the cell and exhibited prominent nucleoli with a fairly loose chromatin pattern and usually a perinuclear halo. The tissues appeared edematous and this seemed to have produced some separation of the cells. About and among these areas of large eosinophilic cells, many straplike and spindle-shaped cells could be seen, some fairly short and plump while others were slender, threadlike cells. Many of these cells appeared to be composed of longitudinal fibrils and on close examination in well-differentiated preparations many of the cells were seen to show definite cross striations (Figs. 3 and 4). As the figures show, these cross striations were demonstrated with equal facility by the phosphotungstic acid hematoxylin technique or the routine hematoxylin and eosin preparations. Connective tissue stains revealed a well-developed fibrous stroma. Large areas of the tumor appeared to consist solely of hemorrhagic, necrotic material and, in these areas, cellular detail had been lost, often the sole surviving cells being a few fibroblasts.

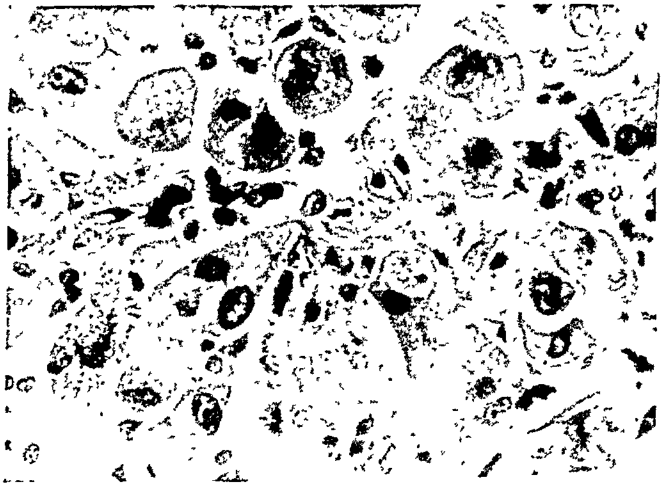

Fig. 2.—Collection of large granular eosinophilic myoblasts. (Hematoxylin and eosin; X150; reduced ¼.)

These large granular eosinophilic cells had the appearance of muscle tumor cells and the finding of cells composed of longitudinal fibrils, which exhibited definite cross striation, confirmed the histologic diagnosis of a tumor of striated muscle. The final diagnosis was rhabdomyosarcoma of the left pleural cavity with atelectasis of the left lung and bronchopneumonia of both lungs.

DISCUSSION

Rhabdomyomatous tumors of the thoracic wall have been described by Stout[12] and Capell[2] and they have also been described within the substance of the lung.[10] Kirshbaum[8] and Perry and Smith[11] have reported the occurrence of malignant striped muscle tumors in the diaphragm, which spread to involve the pleural cavities. Wolfensberger[15] first described an esophageal rhabdomyoma and the 4 previously reported cases of this rare neoplasm have recently been reviewed by DeMuth,[6] who added a fifth. Examples of intrathoracic masses of striated muscle tissue arising in teratomata are seen in the

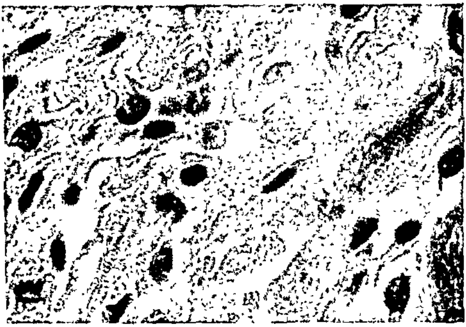

Fig. 3.—Well-defined cross striations in straplike cells. (Hematoxylin and eosin; ×400; reduced ¼.)

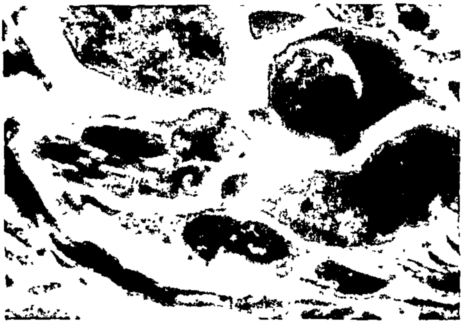

Fig. 4.—Cross striated fibers about large granular myoblasts. (Phosphotungstic acid hematoxylin; ×1,000; reduced ¼.)

reports of Helbing[7] and Zipkin.[17] These observations show that rhabdomyomatous tumors may arise in the region of the pleural cavities, but desipte this an extensive search of the literature has failed to reveal the report of a similar case to that just described. This is, perhaps, not a surprising finding when the unusual occurrence of solitary pleural tumors and the rarity of striated muscle neoplasms in the chest is considered.

The origin of rhabdomyosarcomas has always been a source of interest to histologists. Willis[14] says that striped muscle neoplasms arise either in immature muscle tissue or in multipotent mesenchyme, attempting by this to explain the young age distribution and unusual site of origin of many of these growths. In this case, it was unfortunate that at autopsy it was not possible to define exactly the point of origin of the tumor. However, both Wolfensberger[15] and Capell[2] have commented on the unusual pedunculation which takes place when rhabdomyomatous tumors occur beneath a surface. It seems likely that this tumor arose in either subpleural striated muscle such as diaphragm or in multipotent mesenchymal tissue situated between the lungs or the chest wall and the pleural lining cells. Subsequent pedunculation of the growth, in the same manner as that seen in these other striated muscle tumors, could have produced the final morbid anatomic picture. The intrapleural leiomyosarcoma described by Catron,[4] which resembled the present neoplasm quite closely, seemed to arise in a similar fashion. The absence of any other abnormal tissues from the tumor excluded the possibility of a teratomatous origin for the mass.

A further point of interest lies in the relatively benign character of the neoplasm. Capell and Montgomery[3] consider that those tumors which show well-differentiated myoblastic cells and which develop well-defined cross-striated fibers frequently prove to be the most malignant. The present tumor showed both these features and histologically it was considered to be a malignant neoplasm, yet, despite the fact that the mass must have been present in the patient's chest for many years, no invasion outside the tumor capsule was found at autopsy. Previously Klemperer and Rabin[9] have commented on the apparently benign nature of certain neoplasms when the mass is wholly enclosed within the pleural cavity but they offered no explanation for this phenomenon and none has since been forthcoming.

Consideration of Klemperer and Rabin's work on intrapleural tumors raises the question of the origin and nomenclature of these tumors in general. They recognized two types, a localized connective tissue group and a diffuse malignant epithelial group. They considered that the relatively benign localized connective tissue tumors arose in subpleural tissues and that subsequent growth and pedunculation of the mass produced the intrapleural site of the neoplasm. Recently Stout and Himadi[13] have suggested that all tumors which involve the pleura predominantly arise from pleural lining cells and that they be called mesotheliomas to denote such an origin. For several reasons this concept seems ill founded. It is recognized that tumors, situated within the pleura, initially will produce similar clinical pictures but they do so by virtue of their position not any special kinship between their constituent cells. The natural histories of localized pleural tumors may vary greatly, while those of the diffuse neoplasms consistently exhibit the widest possible variation[1] Many of the reports of supposed primary diffuse pleural tumors on critical examination, prove to be examples of metastasis and confusion of these neoplasms with the localized connective tissue types is common At present, perfectly adequate names are available to denote connective tissue growths to add a further all embracing term to describe them, especially one which embraces such dubious entities as diffuse pleural tumors serves merely to obscure knowledge of their origin The cells lining the pleura are probably of mesenchymal origin and it is possible that they do give rise to tumors[16] but to attempt to force all pleural neoplasms solitary or diffuse, epithelial or mesenchymal into one histogenetic classification appears highly artificial When the tumor possesses clear evidence of its line of differentiation, as in the present case, it is also unnecessary

SUMMARY

A case of rhabdomyosarcoma, solitary within the pleural cavity, is described Its possible histogenesis is discussed and some features of its behavior considered

The nomenclature of pleural tumors is briefly reviewed It is felt that the use of the term "mesothelioma," in the classification of pleural connective tissue tumors, hinders understanding of their nature

My thanks are due to Dr A W Pound for advice and to Dr A D D Pye for permission to use hospital records

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BRONCHOGENIC CYSTS IN INFANTS AND CHILDREN

Jack W. Herrmann, M.D., Theodore C. Jewett, Jr., M.D., and Giovanni Galletti, M.D., Buffalo, N. Y.

PULMONARY cystic disease in children is a subject which demands further clarification, inasmuch as the prognosis is so dependent on early recognition and definitive surgical therapy. Since the appearance of the first article on this subject in America by Koontz[8] in 1925, a great deal of information has been accumulated relative to this pathologic entity. However, in spite of the extensive literature, there is still much confusion concerning the nomenclature and classification of pulmonary cysts. Cooke and Blades[4] tabulated twenty-eight synonyms under which cystic disease of the lung is filed at the Armed Forces Institute of Pathology in Washington, and also collected nine others from the contemporary literature. This multiplicity in terminology is undoubtedly a reflection of how poorly the pathogenesis of this disease is understood.

The classification most generally accepted divides pulmonary cysts into congenital and acquired. This distinction, however, is based on specific histologic criteria; that is, the congenital bronchogenic variety must contain some form of respiratory epithelium in contrast to the acquired group. That this distinction has not been generally accepted is exemplified in an article by Conway,[3] who challenges the congenital origin of many of the pulmonary cysts he studied. Boyd[2] states that the so-called true congenital cyst may lose its characteristic respiratory epithelium following long-standing infection. He also notes that chronic pulmonary abscesses may have an ingrowth of bronchial type epithelium and thus simulate a true cyst.

Most authors believe that pulmonary cysts are derived from the tracheobronchial tree in one of two ways. During the fourth week of fetal life, two septa of epithelial origin divide the primitive foregut into two components. The tracheobronchial tree is derived from the anterior portion while the esophagus originates from the posterior. If cells become detached at this time, growth will continue in an abnormal fashion, resulting in the formation of bronchial or gastrogenic cysts. The other possible developmental defect occurs during the third trimester of fetal life. It is postulated that at this time a bud involving a normal or supernumerary bronchus may be pinched off and separated from the tracheobronchial tree. A pulmonary cyst may then develop in this isolated segment.

From the Department of Surgery, Buffalo Children's Hospital, and the Department of Surgery, University of Buffalo School of Medicine, Buffalo, N. Y.

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All the pulmonary cysts reviewed in this study satisfy the criteria of the congenital bronchogenic variety, inasmuch as their histologic characteristics include some elements of the normal respiratory tract (Fig. 1). We have subdivided these cysts into two main types based upon the presenting symptom complex which they produce, namely respiratory distress or infection. These symptom complexes arise from the complications of pulmonary cysts which have previously been defined by Gross,[7] Ravitch and Hardy,[11] and Allbritten and Templeton.[1] The children in the first category entered the hospital with dyspnea and frequently with cyanosis These signs are the direct result of the space-occupying effect of the expanding lung cyst Children in the second group are examined because of suspected pneumonia, pulmonary abscess, or recurrent bronchitis which actually are manifestations of infection occurring within a cyst. This study comprises a total of 12 patients treated surgically at this hospital during the past 15 years.

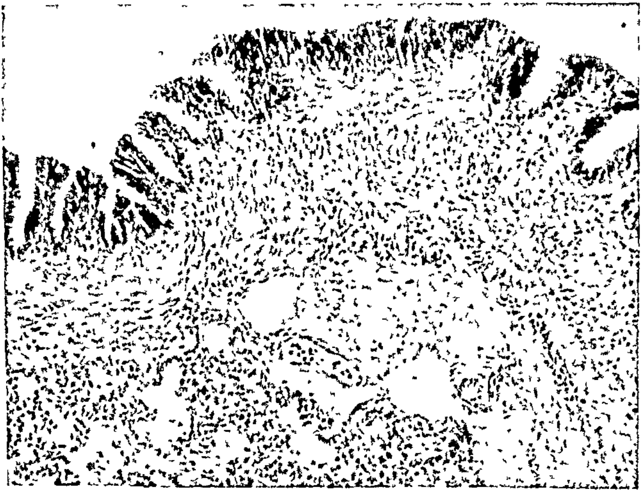

Fig 1—Photomicrograph of bronchogenic cyst showing columnar, ciliated epithelium smooth muscle, and underlying alveoli. Cartilage and lymphoid tissue are not present in this specimen (X165, reduced ⅕)

THE EXPANDING PULMONARY CYST

The development of expanding pulmonary cysts is now a fairly well-understood phenomenon. The essential mechanism for the production of this lesion is a flap-valve type of bronchial or bronchiolar obstruction. As the cyst grows larger, it gradually compresses neighboring tissue and, in an extreme degree, may occupy such a major portion of the hemithorax that the med[illegible]tinum is forced toward the opposite side. This resul [illegible] th[illegible]urrence further unphysiologic states: (1) compression of the contralateral lung and (2) torsion of the heart and great vessels, particularly the venae cavae, with resultant obstruction to the return flow of blood into the right side of the heart. If this process continues unchecked, death from cardiorespiratory causes may follow. Occasionally an expanding cyst may rupture into the pleural space, resulting in a tension pneumothorax, an equally serious situation.

Four of our patients were admitted either as acute or subacute respiratory emergencies. Included in this group were 2 boys and 2 girls. The youngest was 1 day of age, the oldest just under 2 months. All 4 patients entered with the similar history of rapid and progressive cyanosis and dyspnea. The pertinent physical findings were hyperresonance, decreased breath sounds, and evidence of mediastinal shift as noted by the position of the apical heart beat.

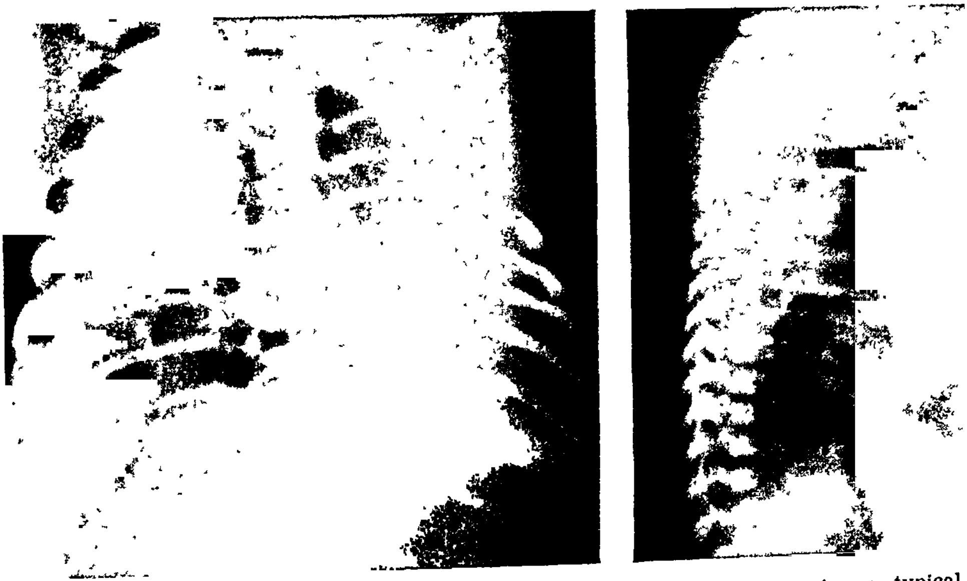

Fig. 2.—Posteroanterior and lateral roentgenograms of the chest showing a typical expanding pulmonary cyst with atelectasis and mediastinal shift.

Although the clinical picture suggested the diagnosis of an expanding cyst, this impression could be confirmed only by careful radiographic study. Roentgenograms (Fig. 2) revealed single or multiple well-circumscribed, thin-walled cystic structures which were occupying part or all of one hemithorax. The cysts partially or completely compressed the adjacent lung parenchyma and demonstrated some degree of mediastinal shift. Other confirmatory signs which indicated the expanding nature of the cyst were depression of the hemidiaphragm and widening of the interspaces on the involved side.

Two lesions which are most difficult to differentiate radiographically from the acutely expanding cyst are a tension pneumothorax and diaphragmatic hernia. It may not be possible to distinguish tension pneumothorax from pulmonary cyst before thoracotomy; however, less harm is done by surgical exploration in this situation than by temporizing with repeated thoracenteses or intercostal drainage. A real effort should be made to differentiate diaphragmatic herniae from pulmonary cysts inasmuch as the former are best corrected in infants through an abdominal approach, whereas the latter can only be attacked by thoracotomy. When the diagnosis is in doubt, the best radiologic technique to prove the presence of a diaphragmatic hernia is by contrast study of the gastrointestinal tract.

The treatment of our 4 cases of expanding lung cysts fairly well exemplifies the changing attitude to this problem in the past decade. Before the advent of the newer techniques of anesthesia and the concomitant advances in thoracic surgery, no attempt was made to attack this emergency directly. Only supportive therapy, consisting of oxygen and needle aspiration of the cyst, was attempted and the resulting mortality was unduly high. In recent years, due to the better understanding of the physiologic problems associated with pulmonary resection, the mortality has been greatly reduced.

Three patients had resections (one pneumonectomy and two lobectomies) with uneventful postoperative courses. The fourth died as a result of an error in diagnosis. This death occurred in an infant who was thought to have a diaphragmatic hernia by roentgenography and consequently underwent laparotomy. Before thoracotomy could be performed, the child suddenly died. This case exemplifies the importance of a correct preoperative diagnosis when multiple pulmonary cysts are present.

The pathology of the resected specimens is summarized in Table I. On gross examination the specimens presented a fairly uniform picture. Single or multiple cysts could be seen lying within the lung parenchyma with surrounding atelectasis. On cross section, they had a smooth, pale, glistening surface with a glary type of mucus on the wall. Some were crossed by fine trabeculae whereas others were multiloculated. A bronchial communication was usually demonstrable; inflammation was not prominent.

TABLE I. EXPANDING LUNG CYSTS

CASE NUMBER	LOCATION	NUMBER OF CYSTS	HISTOLOGY OF CYST WALL
1	RML	One large, numerous small	1. Columnar epithelium 2. Smooth muscle
2	RLL	One large, numerous small	1. Columnar epithelium 2. Smooth muscle
3	RML	Single large	1. Columnar epithelium 2. Smooth muscle
4	LLL	Single large	1. Columnar epithelium 2. Smooth muscle

In the management of the child with an expanding pulmonary cyst, the following points should be stressed. It is essential that the preoperative period occupy as short an interval as possible and be concerned only with making the diagnosis. During the time necessary for carrying out diagnostic procedures, *supportive therapy, mainly oxygen, should be given. Needle aspiration* of a tension cyst plays no part in the definitive treatment of this condition, as shown by Maier and Haight.[9] Thoracentesis should be reserved only for the occasional case which requires emergency decompression until surgery can be performed. Once the diagnosis is made, immediate thoracotomy is mandatory with removal of the expanding cyst. The type of excision may vary from pneumonectomy to segmental resection. The lung should be completely palpated to determine the presence of additional cysts. If the lesions are in the lower lobe, a sequestrated lung should be suspected and a careful search made for the aberrant arterial supply.

THE SECONDARILY INFECTED CYST

The secondarily infected pulmonary cyst occurs as a result of bacterial invasion of a previously sterile cyst. These cysts may be asymptomatic for years, and then suddenly make their presence known in an explosive fashion as an acute inflammatory process. According to Croswell and King,[5] they are originally fluid-filled cavities without bronchial communication and, as such, remain sterile. However, when perforation into a bronchus occurs, bacteria may enter, resulting in secondary infection. Once inflammation has begun, it is difficult to control, since the cavities seldom have dependent drainage. During the acute stage of the infection, there is usually extension of the process beyond the confines of the cysts, resulting in pneumonitis and, at times, empyema. However, on adequate antibiotic therapy, the inflammation may subside, but a nidus remains for later recurrent episodes. Some cysts become a source of chronic pulmonary suppuration with bronchiectasis, and eventually pulmonary insufficiency develops.

Eight cases of secondarily infected pulmonary cysts were evaluated in our study. These children were in an older age group than those with the expanding type of lung cyst. The youngest was 6 months and the oldest 9 years. Of these, 5 were male and 3 female.

These children with the secondarily infected cysts have a classical clinical history of intermittent respiratory infections with asymptomatic intervals. The first attacks are usually interpreted as bronchitis or pneumonia. Following several such episodes, however, roentgenograms of the chest usually reveal the correct diagnosis. The most common symptoms and signs in our patients during the acute stage of their disease were those of pulmonary suppuration, namely, fever, dyspnea, cough, and purulent sputum. Physical findings were not remarkable during the periods of remission, but during the acute attacks they were suggestive of pneumonitis. Laboratory studies of a routine nature only confirmed the presence of infection, and frequently demonstrated a previously unsuspected anemia.

The radiographic picture (Fig. 3) seen in the secondarily infected cyst differed from the expanding cyst in that there was little evidence of compression of surrounding structures. The cysts appeared extremely round, smoothly outlined and thin-walled with varying degrees of pneumonitis and frequent evidence of fluid levels. The latter, however, usually presented with a thicker wall and a great deal more surrounding pneumonitis. A second type of lesion to be considered in the differential diagnosis is the staphylococcal pneumatocele. However, in this disease, pneumonia is the predominant feature. Furthermore, the natural course of this lesion is spontaneous regression over a period of months, which never occurs in the true pulmonary cyst.

The differential diagnosis between the secondarily infected cyst and the previously mentioned pulmonary infections is often extremely difficult and rests in an accurate evaluation of the history, clinical course, and serial roentgenograms. Infected pulmonary cysts characteristically present as acute respiratory infections with relatively asymptomatic intervening periods, whereas, lung abscess entirely resolves without exacerbations or continues as a chronic suppurative process. Roentgenograms may at times be of value in distinguishing these two conditions. This is of some importance, since in recent years excellent results have been obtained in the treatment of the acute abscess with antibiotics.

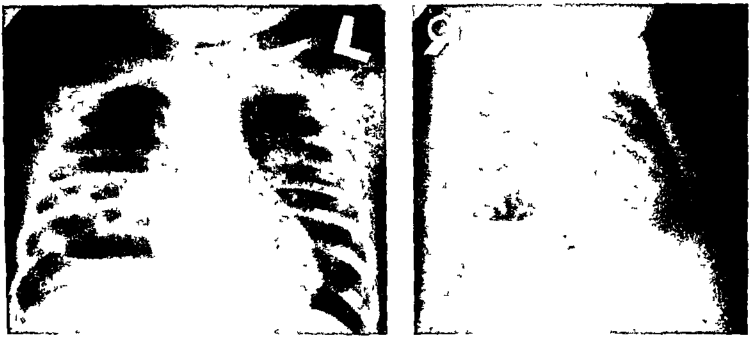

Fig 3—Posteroanterior and lateral roentgenograms of the chest showing the well-circumscribed appearance of an infected pulmonary cyst with a fluid level and minimal surrounding pneumonitis

In contradistinction, infection in a congenital cyst can only be controlled by chemotherapy, but never cured, inasmuch as the underlying cause still remains. Consequently, surgery is the treatment of choice in the latter while conservative means should be employed in pulmonary abscess unless the course of the disease becomes chronic.

The necessity of differentiating the staphylococcal pneumatocele from pulmonary cysts is imperative as shown by the observations of Potts and Riker[10] and Fisher and Swenson,[6] who emphasize that staphylococcal pneumatoceles usually regress spontaneously. Thus, in any case in which the radiographic interpretation is suggestive of lobar ectasia, the history, clinical course, and serial roentgenograms over a period of several months should be reviewed before any thought is given to excisional surgery

The preoperative preparation in children with secondarily infected pulmonary cysts can be divided into two phases, (1) therapeutic and (2) diagnostic. The therapeutic considerations consist mainly of antibiotics to control the infection during the acute stage. Once this has been accomplished, therapy should be directed toward decreasing the tracheobronchial secretions to a minimum by chemotherapy, postural drainage, and bronchoscopic aspiration, if necessary.

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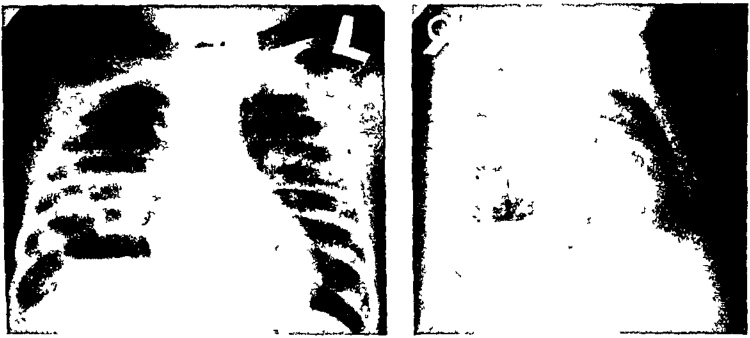

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Blood replacement prior to surgery may be necessary in many of these children with prolonged or recurrent infections. Diagnostic and therapeutic bronchoscopy should always be performed preoperatively to rule out the presence of a foreign body or cystic bronchiectasis. If bronchiectasis is suspected, bronchography should be undertaken to confirm the diagnosis and delineate the extent of the disease.

In the eight infected pulmonary cysts studied, three were treated by pneumonectomy, four by lobectomy and, one of the earliest cases, with marsupialization and subsequent thoracoplasty. There were two deaths in this group; 1 patient died shortly following pneumonectomy after several episodes of cardiac arrest during the procedure and the other patient died on the operating table during right middle lobectomy. Both deaths were attributable to massive flooding of the contralateral lung by infected material from the cysts, and would be preventable deaths today with our present surgical knowledge. These 2 cases emphasize the importance of the proper preoperative preparation aimed at controlling the quantity of secretions in these cysts by antibiotics, postural drainage, and bronchoscopy. The other children in this group had uneventful postoperative courses and have remained well to date.

TABLE II. SECONDARILY INFECTED PULMONARY CYSTS

CASE NUMBER	LOCATION	NUMBER OF CYSTS	HISTOLOGY OF CYST WALL
1	LLL	Multiple small	1. Columnar epithelium
2	RML	One large, multiple small	1. Columnar epithelium 2. Smooth muscle 3. Cartilage 4. Chronic inflammatory reaction
3	RLL	One large	1. Columnar epithelium 2. Smooth muscle 3. Chronic inflammatory reaction
4	LUL and LLL	Multiple small	1. Columnar epithelium 2. Smooth muscle 3. Chronic inflammatory reaction
5	RLL	One large	1. Islands of columnar epithelium 2. Chronic inflammatory reaction
6	RLL	Two large	1. Columnar epithelium 2. Cartilage 3. Smooth muscle 4. Chronic inflammatory reaction
7	RLL	One large	1. Columnar epithelium 2. Smooth muscle 3. Chronic inflammatory reaction
8	RLL	Multiple small	1. Columnar epithelium 2. Smooth muscle 3. Chronic inflammatory reaction

The pathologic findings of these surgical specimens are summarized in Table II. As can be seen, there is a definite predilection for these cysts to occupy the lower lobes. Grossly, they appear similar to the expanding pulmonary cyst except that evidence of infection supplants the signs of compression of neighboring pulmonary tissue. On cross section, the bronchial type mucosa *has a glistening appearance. The cavity itself usually contains purulent* exudate and there is evidence of pneumonitis in the surrounding parenchyma.

Since there is seldom the fulminating life-endangering process occurring in the secondarily infected cyst, as there is with the expanding type, a more *leisurely attitude may and should be taken in the handling of this problem.* It is essential that the proper length of time be utilized to prepare these children adequately for surgery and also to insure the correct diagnosis. This frequently demands time-consuming observations of the clinical course and complete preoperative studies. Once the above requirements have been fulfilled, the indicated pulmonary resection should be performed. The postoperative care is essentially the same as in any child who has undergone thoracotomy.

DISCUSSION

Only 20 years ago Schenck[17] stated that tension type pulmonary cysts were attended by a grave prognosis in infants and children. Acute inflammatory lesions of the lung likewise carried a high mortality during that period. The gloomy outlook has now changed and the prognosis of this disease is excellent as exemplified by the survival of 75 per cent of the patients treated at this hospital by resection. This improvement can be traced, in part, to refinements in surgical technique and care, but more important to the earlier suspicion and consequent diagnosis of this entity. Early recognition of this relatively rare but serious disease can only be accomplished by constantly being alert to its possible existence. Every infant with respiratory distress should have a roentgenogram of the chest to rule out the presence of an expanding pulmonary cyst. Recurrent bouts of pulmonary infection in childhood should be *viewed with suspicion and similar appropriate diagnostic studies undertaken.* Once the diagnosis is established or strongly suspected, excisional surgery is the procedure of choice. If this plan of therapy is followed, children with complicated cystic disease of the lung will come to definitive treatment earlier and the morbidity and mortality will be concurrently lowered.

SUMMARY

1. Congenital pulmonary cysts may be divided into two major groups based upon either of two presenting symptom complexes associated with expansion or infection.

2. Expanding pulmonary cysts are usually found in the newborn period; since they may run a rapidly fulminating course, prompt diagnosis and surgery are mandatory.

3. Infected pulmonary cysts occur in an older age group and usually require a more protracted period for accurate diagnosis and adequate preoperative preparation.

4. The treatment of choice in both types is by resection of the involved pulmonary parenchyma.

Blood replacement prior to surgery may be necessary in many of these children with prolonged or recurrent infections. Diagnostic and therapeutic bronchoscopy should always be performed preoperatively to rule out the presence of a foreign body or cystic bronchiectasis. If bronchiectasis is suspected, bronchography should be undertaken to confirm the diagnosis and delineate the extent of the disease.

In the eight infected pulmonary cysts studied, three were treated by pneumonectomy, four by lobectomy and, one of the earliest cases, with marsupialization and subsequent thoracoplasty. There were two deaths in this group; 1 patient died shortly following pneumonectomy after several episodes of cardiac arrest during the procedure and the other patient died on the operating table during right middle lobectomy. Both deaths were attributable to massive flooding of the contralateral lung by infected material from the cysts, and would be preventable deaths today with our present surgical knowledge. These 2 cases emphasize the importance of the proper preoperative preparation aimed at controlling the quantity of secretions in these cysts by antibiotics, postural drainage, and bronchoscopy. The other children in this group had uneventful postoperative courses and have remained well to date.

TABLE II. SECONDARILY INFECTED PULMONARY CYSTS

CASE NUMBER	LOCATION	NUMBER OF CYSTS	HISTOLOGY OF CYST WALL
1	LLL	Multiple small	1. Columnar epithelium
2	RML	One large, multiple small	1. Columnar epithelium 2. Smooth muscle 3. Cartilage 4. Chronic inflammatory reaction
3	RLL	One large	1. Columnar epithelium 2. Smooth muscle 3. Chronic inflammatory reaction
4	LUL and LLL	Multiple small	1. Columnar epithelium 2. Smooth muscle 3. Chronic inflammatory reaction
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Since there is seldom the fulminating life-endangering process occurring in the secondarily infected cyst, as there is with the expanding type, a more leisurely attitude may and should be taken in the handling of this problem. It is essential that the proper length of time be utilized to prepare these children adequately for surgery and also to insure the correct diagnosis. This frequently demands time-consuming observations of the clinical course and complete preoperative studies. Once the above requirements have been fulfilled, the indicated pulmonary resection should be performed. The postoperative care is essentially the same as in any child who has undergone thoracotomy.

DISCUSSION

Only 20 years ago Schenck[12] stated that tension-type pulmonary cysts were attended by a grave prognosis in infants and children. Acute inflammatory lesions of the lung likewise carried a high mortality during that period. The gloomy outlook has now changed and the prognosis of this disease is excellent, as exemplified by the survival of 75 per cent of the patients treated at this hospital by resection. This improvement can be traced, in part, to refinements in surgical technique and care, but more important to the earlier suspicion and consequent diagnosis of this entity. Early recognition of this relatively rare but serious disease can only be accomplished by constantly being alert to its possible existence. Every infant with respiratory distress should have a roentgenogram of the chest to rule out the presence of an expanding pulmonary cyst. Recurrent bouts of pulmonary infection in childhood should be viewed with suspicion and similar appropriate diagnostic studies undertaken. Once the diagnosis is established or strongly suspected, excisional surgery is the procedure of choice. If this plan of therapy is followed, children with complicated cystic disease of the lung will come to definitive treatment earlier and the morbidity and mortality will be concurrently lowered.

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1. Congenital pulmonary cysts may be divided into two major groups based upon either of two presenting symptom complexes associated with expansion or infection.

2. Expanding pulmonary cysts are usually found in the newborn period; since they may run a rapidly fulminating course, prompt diagnosis and surgery are mandatory.

3. Infected pulmonary cysts occur in an older age group and usually require a more protracted period for accurate diagnosis and adequate preoperative preparation.

4. The treatment of choice in both types is by resection [illegible] involved pulmonary parenchyma.

5. An excellent prognosis can be predicted in this disease with early diagnosis and proper surgical management.

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GIANT INTRATHORACIC LYMPH NODES

Carl B. Mason, M.D., Honolulu, Hawaii

Benign hyperplasia producing giant mediastinal lymph nodes,[1] adds another consideration to the difficult preoperative evaluation of mediastinal masses and is particularly important because, both grossly and histologically, it may be mistaken for a thymic tumor. Because of the possible relationship of thymic function and thymic tumors to the crippling disease, myasthenia gravis, such an error may be harmful to a patient and might confuse the further study and classification of this problem. Furthermore prognosis for the lesions may vary.

Castleman and associates[2] reported a case of benign hyperplasia of mediastinal lymph nodes and Castleman, Iverson, and Menendez[3] collected 13 cases from an extensive study of thymic tumors. Etiologically, they favor chronic inflammation rather than new growth of thymic origin. The initial diagnoses of ectopic thymic tumor in 1 case[4] and primary subpleural thymoma in another[5] were changed to benign hyperplasia of lymph nodes upon review.

In most cases a routine or survey film of the chest discloses an asymptomatic mass protruding from either lung hilum or occupying the anterior mediastinum. Surgical excision is usually simple and not followed by recurrence or complication. The gross specimen usually presents a firm, well encapsulated mass with a finely granular cut surface. Microscopically, there is marked lymphoid hyperplasia with capillary proliferation in various stages. Often there are highly reactive germinal centers with hyalinization and lymphocytic cuffing. These may closely resemble the Hassall's corpuscles of the thymus and thereby may lead to an erroneous diagnosis.

CASE REPORTS

CASE 1*.—Chinese male, 23 years old. An asymptomatic left hilar mass gradually enlarged as demonstrated in chest films over a 3 year period (Fig. 1). All preoperative examinations, including sputum studies for bacilli and cells, tomograms, bronchoscopy, and angiocardiography failed to clarify the diagnosis. In September, 1954, a left thoracotomy demonstrated an egg sized mass in the interlobar fissure of the left hilum, with no invasion into the surrounding lung parenchyma. The mass shelled out easily as it was well encapsulated.

From the Department of Surgery, Leahi Hospital, Honolulu, Hawaii.
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*Case from the service of Dr. Paul W. Gebauer.

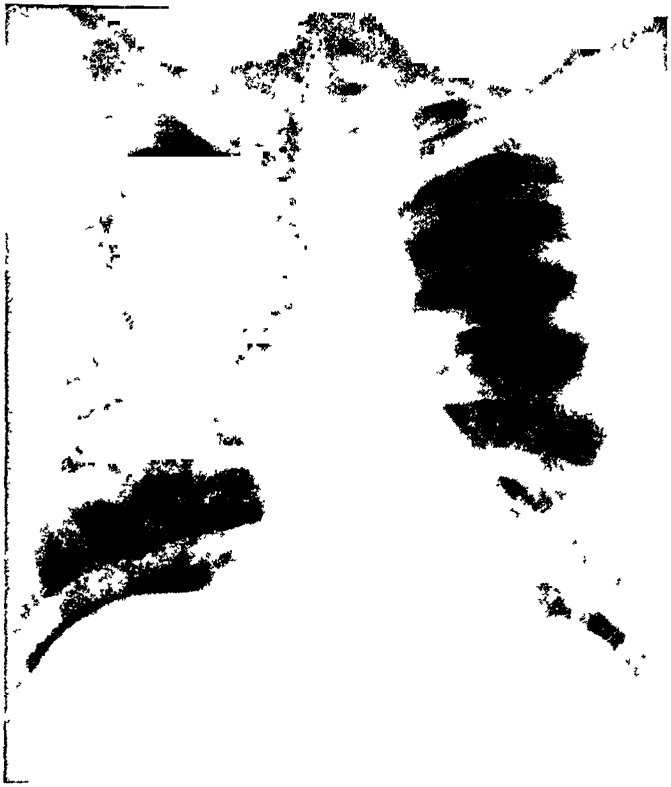

Fig. 3.—A small, circumscribed right hilar mass is seen in the posterior-anterior chest film.

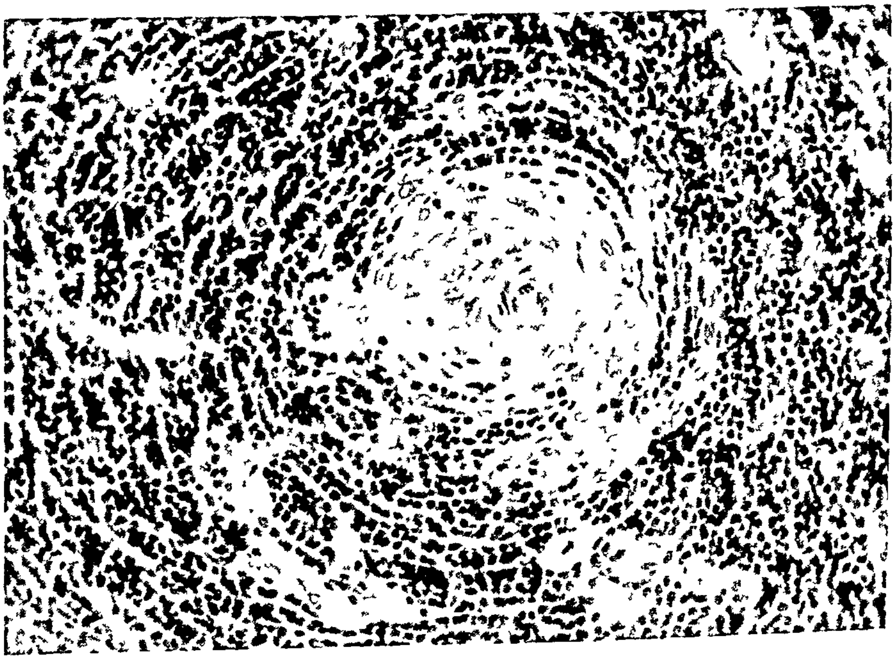

Fig. 4.—Histologic examination section shows the so-called "pseudo-Hassall corpuscles," consisting of the epithelioid cell masses and hyaline characteristic of hyperplastic lymph nodes.

of thymocytes and reticular cells; the latter tend to form pseudo Hassall corpuscles. There is some tendency toward rosette formation of thymocytes. The picture is that of thymoma and is benign. There are hyaline bands between the lymphoid cells This is rather characteristic of this particular lesion. Diagnosis: Benign thymoma.''

In August, 1957, after reviewing all thymomas removed at Queen's Hospital, the same pathologist reported· ''Review of this slide in view of later knowledge leads me to class this an a localized hyperplasia of a mediastinal lymph node and still benign The previously *called thymocytes are lymphocytes, undoubtedly* This case has been *removed from* the thymoma classification. Amended diagnosis: Localized hyperplasia of a mediastinal lymph node ''

CASE 3*.—Filipino male, 49 years of age. A yearly survey film of the chest revealed a mass in the anterior mediastinum, which was asymptomatic and had been present for about 1 year. Preoperative sputum studies, angiocardiography, and bronchoscopy revealed *no abnormality.* The preoperative diagnosis was thymoma or dermoid In August, 1957, a left thoracotomy revealed a 6 cm mass lying beneath the mediastinal pleura, superior to the pulmonary artery and anterolateral to the ascending thoracic aorta. The mass easily shelled out, with no evidence of local invasion. Frozen section studies revealed either ''lymphoma or thymoma ''

The pathologic report was as follows· ''The specimen consists of a mass, well encapsulated, ovoid in shape, measuring 8 cm. in its greatest dimension and 6 cm. in its least *dimension. Weight 100 Gm Cut section reveals a lobular pattern and an attempt at* lobular formation Areas of subcapsular hemorrhage are seen Histological examination reveals a markedly enlarged lymph node, which shows severe hyperplasia of both lymphoid and reticular elements, but with good preservation of the architecture Normal germinal centers, small vessels, and peripheral sinuses are noted The cells are well differentiated and uniform No thymic elements can be seen The picture is that of an unusually marked but benign hyperplasia, presumably of inflammatory origin Diagnosis: Mediastinum, benign hyperplasia of lymph node ''

However, after multiple sections and further studies by numerous pathologists, in a supplementary report the diagnosis was changed to ''Mediastinal tumor, thymoma, most likely benign.''

SUMMARY

These cases illustrate the salient clinical and pathologic features of giant intrathoracic lymph nodes and demonstrate the necessity of thoracotomy for diagnosis. The second case suggests that histologic review of thymomas by pathologists might disclose more instances of benign hyperplasia and help clarify the difficulties existing in their diagnosis and identification. Case No. 3 is a case in point which illustrates the difficulty in the differentiation of benign hyperplasia of lymph nodes from thymic tumors All of the cases indicate the importance of careful study of a given lesion for accuracy so that behavior, treatment results, and prognosis may perhaps be clarified

The writer wishes to thank Dr P. W. Gebauer for his assistance in this paper, Dr I L Tilden for the photographs of the histologic sections, and Mr. I. Ota for the chest pictures.

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CONGESTIVE ATELECTASIS: A FATAL POSTOPERATIVE COMPLICATION

Hurst B. Hatch, Jr., M.D., and G. M. Carrera, M.D., New Orleans, La.

Since the original description, by Jenkins and associates,[1] of postoperative congestive atelectasis, this complication has received little attention in the medical literature. It probably occurs more often than this scarcity of reports would indicate. We became interested in this condition about 4 years ago, when we encountered our first patient with this complication. The clinical picture presented by this patient was one of sudden onset of severe dyspnea, deep cyanosis, fever, labored expiratory breathing, tachypnea, tachycardia, and hypotension, aggravated by infusion of fluid, particularly blood. There were no pathognomonic roentgenographic signs. The condition was characteristically resistant to all forms of therapy directed toward pulmonocardiac failure. Since then we have seen 6 additional patients in whom this condition developed after a thoracic surgical procedure. It is the purpose of this report to call attention to this entity by discussing it in the light of our experience with these 7 cases.

Congestive atelectasis is a complication of parenteral fluid therapy. These complications may be grouped into four major types: (1) pyrogenic reactions, (2) volume variations, combined with changes in osmolar concentration, (3) compositional disturbances, and (4) "speed" reactions. Predominantly, congestive atelectasis is a complication of the fourth type.

This entity was described by Bert[2] as attending rapid decompression. The description of the gross and microscopic findings of the lung in rapid decompression, as reported by Fegler and Banister,[3] is almost identical with those described by Muirhead,[4] of patients receiving large amounts of intravenous fluids rapidly. Grossly, the lungs of congestive atelectasis are heavy, and macroscopically the condition suggests gross hemorrhage. The areas affected are sharply limited; they are liver-like, uniform, and dark red. The affected portions seem to be commoner around the hilum and on the dorsal surfaces of the lungs. Microscopically, intense capillary congestion, intra-alveolar hemorrhage, minimal pulmonary edema, and incomplete expansion of pulmonary tissue are seen.

From the Departments of Internal Medicine and Pathology, Ochsner Clinic, New Orleans, La.

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In addition to the excessive and rapid infusion of fluid, probably other factors contribute to development of this complication. Physical injuries, such as surgical procedures, burns, blast injuries, anaphylaxoid shock, or pre-existing shock from some other cause, are the most common. However, none of these alone would necessarily be the cause of death.

The onset of congestive atelectasis is sudden. The dyspnea is severe and indicative clinically of an expiratory obstructive type of breathing. The cyanosis is deep and resistant to all forms of therapy. The tachycardia and hypotension are pronounced and progressive.

The physical signs are those usually found in a patient with acute left ventricular failure. However, in some cases the classical findings of acute left ventricular failure, particularly multiple moist râles throughout the pulmonary field, are absent.

Probably one of the more frequent surgical complications is obstructive collapse of pulmonary tissue. This complication should not be confused with congestive atelectasis, as the two conditions differ, not only in their clinical manifestations but also in their response to therapy. In Table I comparison of the four major physical findings is shown.

TABLE I. DIFFERENTIATION BETWEEN OBSTRUCTIVE AND CONGESTIVE ATELECTASIS

PHYSICAL FINDING	OBSTRUCTIVE	CONGESTIVE
Cyanosis	Light	Deep
Response to oxygen	Good	Poor
Mediastinal shift	Present	Absent
Bronchoscopy	Helpful	Not helpful

Characteristically, all known treatment has been futile. Administration of digitalis and oxygen, and performance of phlebotomy and bronchoscopic aspiration have been to no avail. Inhalation of carbon dioxide, frequent turning of the patient, administration of steroids, and coughing have had no beneficial effect. Despite all known resuscitative measures, the fully developed syndrome is always fatal.

In our 7 patients there were two common factors: (1) rapid infusion of large amounts of fluid during and after a surgical procedure, and (2) a thoracic operation. Six of our patients were men and 1 was a woman. Their ages ranged from 44 to 65 years. Since the pattern in all 7 cases was similar, only one will be reported in detail.

REPORT OF CASE

A white man, aged 44 years, was admitted to Ochsner Foundation Hospital in July, 1956, because of hemoptysis of 1 week's duration. At the age of 11 years, after tonsillectomy, an abscess developed in the right upper lobe of the lung. Empyema subsequently developed and this was drained.

No abnormalities were detected on physical examination the day of admission. Results of routine laboratory studies were within normal limits. In roentgenograms of the chest, retraction of the transverse fissure superiorly, with a radiolucency, 2 cm. in diameter, and some haziness surrounding this area of radiolucency in the anterior segment were noted. In planograms, definite cavitation was seen in the anterior segment of the upper lobe. On bronchography, an outline of the cavity in the anterior segment was seen with cystic bronchiectasis in the right upper lobe.

Right upper lobectomy was done. Within 4 hours the patient received 2,500 c.c. of blood and 2,000 c.c. of glucose in water. Soon after his return from the operating room he had an acute hypotensive episode accompanied by progressive dyspnea and severe cyanosis with pronounced tachycardia. Because of the severe hypotension, within 17 hours the patient received 9,000 c.c. of whole blood, of which 1,500 c.c. had been transfused at a rapid rate. Despite all efforts to reverse the hypotension, the patient died 24 hours after operation.

The gross and microscopic pictures (Fig. 1) were typical of congestive atelectasis.

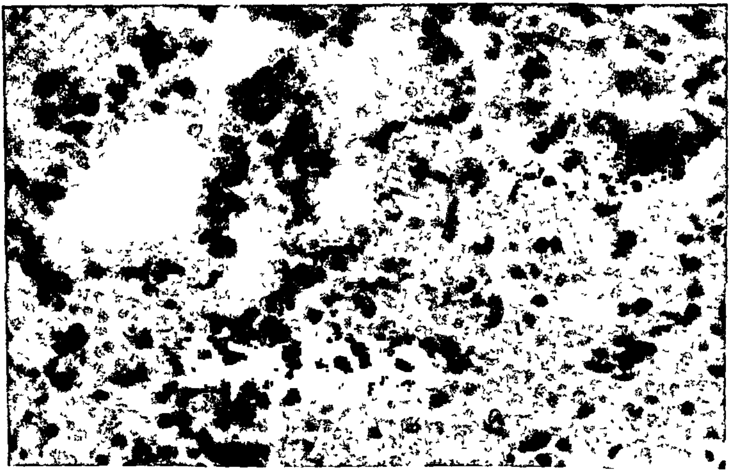

Fig 1.—Case 1. Lung. There is extensive congestion of the capillaries in the alveolar septa, with some extravasation of red blood cells. The alveolar spaces show compression by the congested, edematous parenchyma, and contain coagulated protein and red cells. (Hematoxylin and eosin, ×430, reduced ¼.)

DISCUSSION

The experimental studies of this condition by Moyer[5] are fascinating. He reproduced, in animals, every manifestation of congestive atelectasis noted in human beings except the severe hypotension. He concluded that his experimental findings did not completely clarify the etiology of non-decompression atelectasis. However, his studies have contributed to some understanding of the phenomenon. Several facts are apparent from his work. First, the volume of blood in the lungs increases rapidly after hemorrhage or asphyxia and, second, stiffening of the lung begins soon after rapid parenteral injection of solutions, even in an animal which is not in shock. He noted that the stiffness became pronounced as the left atrial pressure fell. This rules out left ventricular failure as a universal cause of acute development of pulmonary stiffness postoperatively.

Physiologically, an initial rise is followed by a drop in the pulmonary arterial pressure. Then, a fall in systemic pressure occurs and is progressive; the residual air decreases and the respiratory rate increases. As evidence of stiffness or loss of compliance in the lungs, the tidal volume is decreased or is unchanged even as the inspiratory intrapleural pressure becomes more negative than the expiratory intrapleural pressure becomes more positive, thus increasing the work of breathing. It is apparent that the cyanosis represents continuance of pulmonary blood flow through the capillary area in the presence of airless alveoli, a definite abnormality of ventilation and perfusion.

Since our experience with this syndrome, we have been extremely cautious in the postoperative administration of parenteral fluids. Obviously, the best therapy for this fatal syndrome is preventive. In all patients in whom hypotension develops postoperatively, it is imperative to determine the cause, if possible, and treat it physiologically rather than to rely on infusion of fluids to raise the blood pressure to an accepted clinical level. Since low blood pressure is a sign of disease, we are actually treating the effect rather than the cause of the disease. Every hypotensive episode occurring during or immediately after operation is not necessarily due to loss of blood.

SUMMARY

Congestive atelectasis, or acute pulmonary congestion, a little known postoperative complication, is discussed in the light of experience with 7 cases. We believe that this complication is preventable. It is hoped that this report will stimulate the clinician to determine the cause of shock and thus treat it physiologically rather than mechanically.

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INTRATHORACIC MENINGOCELE

Hiram D. Hilton, M.D., Lincoln, Nebr., and Harry H. McCarthy, M.D.,** Omaha, Nebr.*

INTRATHORACIC MENINGOCELE was first described in the literature by Pohl in 1933. The next recorded surgical attack was carried out by Ameuille and associates in 1940. The meningocele was excised, and the resulting defect packed. A spinal fluid fistula and an empyema combined to produce a fatal issue.

Isolated case reports and reviews of the literature have appeared from time to time, the latest being that of Raison. According to our own computation, there have been 27 verified cases reported in the world literature to date, making the patients reported in this communication the twenty-eighth and twenty-ninth, respectively (Table I). Data are incomplete in some case reports. These include the case of Freedlander, the case seen incidentally at necropsy by Kay, the case of Head (quoted by Baker and Curtis, and Raison), 1 case of Byron and associates, and that of Ottani (quoted by Raison).

Surgical correction has been undertaken in 14 patients. Four have died from causes related directly to surgical intervention. The first 2 cases reported were surgical fatalities. Since 1948, however, there have been 12 operations with 2 deaths (Table II).

The etiology of intrathoracic meningocele is, of course, speculative, and numerous explanatory theories have been postulated. It could represent the result of a primary defect in the posterior neural arch. Abnormal extension of the dura around the emerging spinal nerves is another possibility. Localized disease of the dura might conceivably render it too weak to resist pressure of the subarachnoid space, resulting in saclike dilatations of the intraspinal meninges through an enlarged intervertebral foramen. The frequent association of this entity with neurofibromatosis is striking, and may be significant. Fifteen of the 27 cases reported in the literature have been associated with neurofibromatosis. Some authors, in fact, consider intrathoracic meningocele simply to be one manifestation of von Recklinghausen's disease. Neurofibromatosis is known to be characterized by developmental disturbances in neural tissue and occasionally by bony changes, including scoliosis and

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*Clinical Assistant Professor of Surgery, College of Medicine, University of Nebraska, Lincoln, Nebr.

**Professor of Surgery, Creighton University School of Medicine, Omaha, Nebr.

TABLE I

AUTHOR	SEX	AGE	CUTANEOUS NEUROFIBROMATOSIS	SITE OF ORIGIN	OPERATION	REMARKS
Pohl (1933)	F	47	Yes	D3-4	Yes	Died of empyema
Schuller and Uiberall (1938)	M	56	Yes	D7-8	No	Died following resection of posterior roots 6, 7 and 8
Ameuille et al. (1940)	F	48	No	D8-9	Yes	Died of empyema and spinal fluid fistula
Freedlander (1946)	F	?	Yes	?	Yes	?
Singpiel et al. (1947)	M	21	No	D1-2	No	
Mendelsohn and Kay (1948)	F	40	Yes	D7-8	Yes	Recovery
Kay	One case seen incidentally at autopsy					
Welch et al. (1948)	F	41	Yes	D6-7	Yes	Recovery
Byron et al. (1948)	F	36	No?	D2-3	Yes	Recovery
	M	61	Yes	C7-D1	Yes	Died from hemorrhage
	M	21	No	D1-2	No	
Head (1948)	M	43	No	?	No	
Cross et al. (1949)	M	22	Yes	D8-9	No	
Ciaglia (1952)	F	31	Yes	C7-D1	Yes	Recovery
Rubin and Stratemeier (1952)	?	7 wks.	No	D4-5	No	Died
Baker and Curtis (1953)	F	40	Yes	D8-9	Yes	Recovery
	M	63	No	D9-10	Yes	Recovery from operation, but died 7 months later of Paget's disease
ears et al. (1953)	F	29	No	D2-3	Yes	Recovery
Kessel (1951)	F	23	Yes	D5-6	Yes	Recovery
	F	8	Yes	D7-8	Yes	Operation done to relieve paraplegia; resection of vertebral body only
Turunen (1953)	M	33	Yes	D5-6	Yes	Recovery
Ottani (1951)	Incomplete data—proved by aspiration					
Hackenseller (1953)	F	45	Yes	D8-9	No	Died following irradiation therapy
Portigliatti-Barbos (1953)	F	60	Yes	D6-7	No	Died following coughing spell
Gernez-Rieux and Lepaul (1954)	M	59	No	D11-12	No	
Raison (1956)	M	39	No	D8-9	Yes	Recovery
	F	46	Yes	D3-4	Yes	Died from cerebrospinal leakage

TABLE II SURGICAL TREATMENT OF MENINGOCELE

AUTHOR	OPERATION	RESULTS
Pohl (1933)	Myeloplasty	Died of empyema
Ameuille et al (1938)	Packing	Died of empyema and spinal fluid fistula
Mendelsohn and Kay (1949)	Myeloplasty	Recovery with satisfactory result
Welch et al (1948)	Myeloplasty	Recovery with satisfactory result
Byron et al (1949)	Myeloplasty	Recovery with satisfactory result
	Myeloplasty	Died from hemorrhage during operation
Kessel (1951)	Myeloplasty	Recovery with satisfactory result
Ciaglia (1952)	Myeloplasty	Recovery with satisfactory result
Baker and Curtis (1953)	Myeloplasty	Recovery with satisfactory result
	Myeloplasty	Recovery from operation but died 7 months later of Paget's disease
Sears et al (1953)	Myeloplasty	Recovery complicated by spinal fluid fistula and meningitis, ultimate recovery with good result
Turunen (1953)	Myeloplasty	Recovery with satisfactory result
Raison (1956)	Myeloplasty	Recovery with satisfactory result
	Myeloplasty	*Died from spinal fluid fistula*
Hilton and McCarthy	Myeloplasty	Recovery with satisfactory result

growth abnormalities The fact remains, however, that intrathoracic meningocele can and does exist independently of neurofibromatosis A relationship undoubtedly exists, but its causal nature is open to question

Deformities of the thoracic spine ordinarily accompany an intrathoracic meningocele In fact, 23 of the 27 cases reported manifest vertebral abnormalities adjacent to the tumor For the most part, they are consistent with pressure effects exerted by the cystic mass Vertebral changes commonly observed include kyphosis, scoliosis, kyphoscoliosis, erosion or destruction of vertebral pedicles Occasionally, the ribs contiguous to the meningocele are spread, resulting in subluxation of the costovertebral articulation The intervertebral discs are unaffected

Neurofibromatosis is seldom associated with posterior mediastinal neurogenic tumors Kent and Blades ascertained from a large series that this combination is so infrequent that it is statistically of no significance

There is no constant or characteristic symptomatology related to intrathoracic meningocele A survey of the literature indicates that some individuals seek medical advice for a variety of reasons, including pain in the chest, shoulder, and thoracic spine, persistent unexplained coughing, and intractable headache Others become apprehensive about a progressive spinal deformity

Many are asymptomatic, a posterior mediastinal tumor having been divulged by a roentgenogram of the chest taken during the course of a complete physical examination.

Since intrathoracic meningocele is a rare entity, it is seldom suspected and, therefore, almost never diagnosed preoperatively. A posterior mediastinal tumor discovered in a patient with von Recklinghausen's disease should, however, lead one to suspect it. If, in addition, there are associated skeletal changes one may confidently predict it. Only myelography demonstrating a passage of the contrast medium from the subarachnoid space into the mass can confirm it.

Fig 1

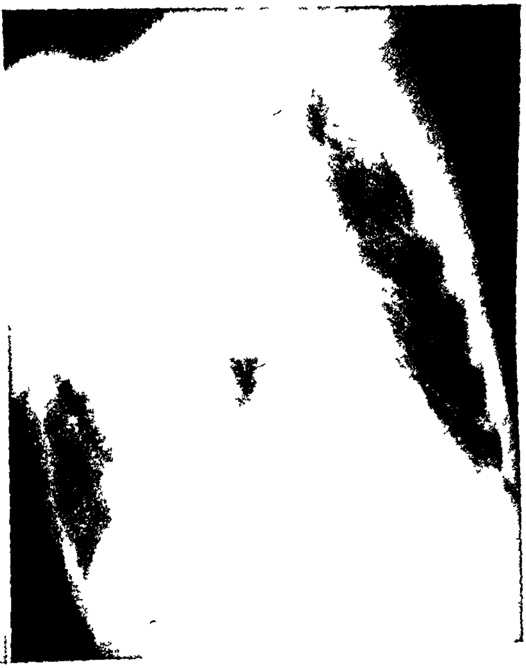

Fig 2

Fig. 1.—Anteroposterior roentgenogram of the chest in Case 1 demonstrating a mediastinal mass projecting into the right hemithorax.

Fig. 2.—Lateral roentgenogram of the chest in Case 1 demonstrating the posterior situation of the mediastinal mass.

Because intrathoracic meningocele represents a progressively expanding lesion, subject to rupture and prone to pressure effects upon surrounding structures, the treatment of choice is surgical repair of the defect. This is done through a posterolateral thoracotomy incision. The dural sac is dissected free from the pleura and adjacent structures until the dilated intervertebral foramen is encountered. It is then opened and trimmed, taking care to leave enough dura for the repair. The dura and its overlying pleura are then imbricated separately so as to give a firm and water-tight closure. It is probably prudent to place an intercostal catheter in the pleural space for the application of continuous suction for 24 hours postoperatively. In this way, complete re-expansion of the lung is assured and the dural repair reinforced.

Postoperative mortality and complications are derived from infection (meningitis and empyema) and spinal fluid leakage with fistula formation Meticulous aseptic technique should forestall the development of the former and careful closure of the defect of the latter If spinal fluid leakage does occur, the recommended procedure is to keep the patient at bed rest and do daily spinal fluid taps so as to decrease the spinal fluid pressure

CASE REPORTS

Mr G M T, a 44 year old white man, gave a long standing history of intractable headaches Nausea frequently accompanied the onset which usually occurred during the night Postural change, particularly lying down, seemed to precipitate an attack or to aggravate one already established Medication for pain was of little or no avail, the

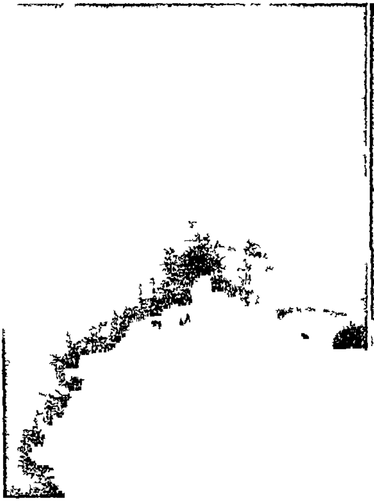

Fig 3

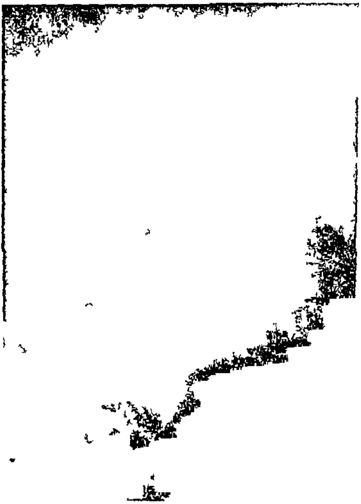

Fig 4

Fig 3 —Anteroposterior roentgenogram of the chest showing opacity in the right lower hemithorax in Case 2

Fig 4 —Lateral view of the right hemithorax in Case 2 showing meningocele

greatest amount of relief being obtained by getting up and about In fact, a headache would frequently subside after a day's activity During the past 3 years the patient had noted intermittent twitching of the eyelids and the right side of the face

Physical Examination—The skin of the thorax was the site of multiple cutaneous fibromata and areas of pigmentation Intermittent twitching of the eyelids and muscles of the right side of the face was noted

Roentgenographic Examination—Posteroanterior and lateral chest films revealed a tumor in the posterior mediastinum projecting to the right The mass measured [illegible] cm in diameter, was smooth in contour, and extended from the [illegible] to the [illegible] There was considerable decalcification and spreading of the [illegible] portion of [illegible] and eighth ribs on the right There was slight [illegible] convexity [illegible]

Diagnosis.—Neurogenic tumor of the posterior mediastinum.

Operation.—Exploration of the right pleural cavity revealed a large cystic mass occupying the mid-portion of the posterior mediastinum. The overlying pleura was dissected away from the cyst so as to gain adequate exposure. Dissection was carried down to an enlarged intervertebral foramen between T_5 and T_6. The cyst was then opened, spinal fluid evacuated, and the spinal cord amply visualized. The cyst wall, consisting of dura, was then trimmed, taking care not to sacrifice too much tissue. The enlarged intervertebral foramen was closed by imbricating the dural flaps, using 3-0 interrupted silk sutures. The dural repair was reinforced by imbricating the mobilized pleura in the same manner. Two No. 34 mushroom intercostal catheters were left in place for application of continuous suction during the immediate postoperative period.

Fig. 5.—Photograph showing open hemithorax and meningocele prior to surgical repair.

Postoperative Course and Follow-up.—The patient's convalescence was uneventful. Eighteen months following surgery he reports definite diminution of the severity and frequency of headaches.

Mrs. B. A., a 37-year-old white woman, was admitted to the hospital for diagnosis and treatment. An opacity had been disclosed in the right lower hemithorax some months before as a result of a routine chest survey. She had noted some weakness in the right leg for several years. This had resulted in a slight limp. However, she had experienced this for so long a period of time that she paid little or no attention to it.

Physical Examination.—Slight weakness of the right leg was noted. Knee jerks were, plus 3 on the right, plus 1 on the left. Ankle jerk was absent on the right, present on the left.

Roentgenographic Examination.—Chest film revealed a round density measuring 6 cm. in diameter located just to the right of the vertebral column. There was some destruction of the bodies of T_{10} and T_{11}.

Diagnosis.—Neurogenic tumor, dumbbell type, arising in the posterior mediastinum.

Operation.—Exploration of the right pleural cavity revealed a large, rounded cystic mass communicating with a defect between the tenth and eleventh ribs. A small bridge of bone was present beyond which another sacular mass protruded. The meningocele was dissected free down to the neck of the sac which measured approximately 1.5 cm. in diameter. Upon opening the first meningocele, the second collapsed much as a pantaloon inguinal hernia would do. The edges of the resected sac were carefully imbricated with interrupted silk sutures. The larger meningocele was then excised at the neck and closed with two rows of 3-0 silk sutures, one row of mattress and the other row interrupted on the free edge. Two mushroom catheters were placed in the right hemithorax. These were connected to underwater suction drainage.

Postoperative Course and Follow-up.—The postoperative course was entirely uneventful. There is no evidence of recurrence of the meningocele over 1½ years after surgery, and the weakness noted preoperatively in the right lower extremity has not progressed.

Fig. 6.—Photograph showing opened meningocele in Case 2 in preparation for surgical closure.

SUMMARY

Intrathoracic meningocele is an anomaly usually associated with neurofibromatosis and typical skeletal changes affecting the thoracic vertebrae. The condition may be suspected or even anticipated whenever a posterior mediastinal tumor occurs in conjunction with skeletal changes and neurofibromatosis. The treatment is surgical, since it represents an expanding lesion. Reference is made to Table I and Table II for a summary of the cases encountered in the literature to date.

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Discussion of Two Meeting Papers

CREATION OF A TEMPORARY ARTIFICIAL DUCTUS FOR THE SURGICAL CORRECTION OF VENTRICULAR SEPTAL DEFECTS ASSOCIATED WITH SEVERE PULMONARY HYPERTENSION BY HOWARD D. SIRAK, M.D., AND DON M. HOSIER, M.D., COLUMBUS, OHIO,* AND CORRECTIVE SURGERY IN THE PRESENCE OF FAR-ADVANCED PULMONARY HYPERTENSION BY C. WALTON LILLEHEI, M.D., DONALD J. FERGUSON, M.D., AND RICHARD L. VARCO, M.D., MINNEAPOLIS, MINN.†

DR. WILLIAM H. MULLER, Jr., Charlottesville, Va.—Both of these are important papers because, as they indicated, pulmonary hypertension is one of the major problems that one faces in corrective surgery for congenital heart disease. About 5 years ago, Dr. Kattus and I had planned to use a decompressing shunt from the aorta to the pulmonary artery when we were closing a large ductus with reversal of blood flow. Fortunately, we were able to close it without performing a shunt. I am delighted to see that Dr. Sirak has utilized it with a high degree of benefit in his patients.

I would like to mention one other approach in the management of pulmonary hypertension in patients with congenital heart disease, that is, a procedure to narrow the main pulmonary artery in certain patients who have a physiologic single ventricle and severe pulmonary hypertension. This procedure was initiated before total cardiopulmonary bypass and open-heart surgery was being done. The indications for it at that time, in our opinion, were rather broad. We advocated its use to prevent the development and progression of luminal narrowing resulting from medial hypertrophy and intimal fibrosis of the small muscular pulmonary arteries and arterioles of the lung, as was shown in both these patients, and to control high output failure in small infants. We now think that its chief indication is in the small infant with a ventricular septal defect or a single ventricle where the mortality rate of a corrective open-heart procedure in our hands, and I believe in others, is excessive. At the present time, it is the only treatment I know of for a single ventricle, although correction of this defect has been tried unsuccessfully with total bypass. It may also be used in the older child who has passed from a balanced phase to an early right-to-left shunt, where the mortality rate from a corrective procedure may also be high.

Work in our research laboratory by Dr. Richard H. Blank appears to indicate that severe pulmonary vascular changes, which we have hitherto thought were permanent, are reversible. It is possible, therefore, that after a period of time patients who have had narrowing of the pulmonary artery may be able to have a corrective open-heart operation with a lower mortality rate.

(slide) This slide demonstrates a very large pulmonary artery and a small aorta, as we usually find it in these patients. (slide) Here, the main pulmonary artery is narrowed by suturing a band of synthetic fabric about it. We initially removed a segment of the circumference of the artery but now rely totally on the band.

One of the critical points of this operation is the degree of narrowing, and we find that the lumen of the artery must be reduced to one third of its previous size in order to obtain the necessary reduction in pulmonary blood flow. This may best be determined by measuring the pressure proximally and distally to the point of stenosis. While a normal pulmonary artery pressure is not often tolerated by the heart in most instances, it can be reduced from 30 to 40 mm. Hg. If this degree of pressure reduction is not obtained, the desired clinical improvement in the patient does not usually follow.

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*Published in January 1959 issue, pages 1-21

†Not yet published.

DR. CHARLES P. BAILEY, Philadelphia, Pa.—My discussion concerns not only these two papers but also, perhaps in anticipation, Dr. Kirklin's paper on the tetralogy of Fallot. We have been troubled not only by the operative mortality in cases of ventricular septal defect with pulmonary hypertension but also by the surprisingly high operative mortality which attends correction when there is no pulmonary hypertension. You have just heard Dr. Sirak's suggestion for the elective creation of a patent ductus arteriosus and acceptance of a two-stage procedure because he is having similar difficulties. Dr. Effler has described acute left atrial hypertension after definitive closure of defect and restoration of the heartbeat. It occurred to us that this might be related to the suddenness with which we altered the cardiac physiology. It seemed to us that it would be better if the defect, and hence the shunt, were closed off gradually.

(slide) Following the line of thought presented last year by Dr. John Lewis, we created a prosthesis made up of two attached slices of compressed Ivalon sponge, one of which is perforated centrally. This we call a prosthetic artificial foraminal valve. At first we thought of it only to permit continuation of the right-to-left shunt in a case of the tetralogy of Fallot completely corrected. This would tend to prevent engorgement of a hypoplastic pulmonary vascular bed.

We have applied this prosthetic valve in atrial septal defects, as you see from this case, with a large common atrioventricular canal. The defect measured 1½ in. by 1¼ in.

Some time ago we had the experience of observing a rise in the left atrial pressure to 80 mm. Hg, with ensuing death, in a patient with an uncomplicated ventricular septal defect immediately after closure and restoration of circulatory integrity. Effler and Dodrill have had similar experiences in which the left atrial engorgement was followed by uncontrollable acute hemorrhagic pulmonary edema. It occurred to us that the artificial foraminal valve could also be applied in such a manner as to permit a continuation of a pre-existing left-to-right shunt.

These prosthetic valves placed in an experimental animal are closed by sealing together of the leaves within 8 weeks. We think that Dr. Lillehei's suggestion as to a perforated Ivalon disc is particularly pertinent in cases of pulmonary hypertension with a nearly "balanced" shunt. However, in patients with the tetralogy of Fallot and in those with uncomplicated ventricular septal defect with unidirectional shunt, we feel that it is preferable to use a unidirectional valve of this type to provide immediate maintenance and gradual decrease of the one-way shunt until its final obliteration. After all, does it matter whether we cure the patient in 5 minutes or in 8 weeks? So far we have had one death in the application of this technique in 8 patients.

DR. OSLER ABBOTT, Emory University, Ga.—This discussion was not returned.—EDITOR.

DR. FRANK L. GERBODE, San Francisco, Calif.—I would like to discuss Dr. Lillehei's paper and to compliment him again on pointing the way in this particularly difficult field of pulmonary hypertension. I would like to ask whether he believes that the type of pulmonary hypertension found in patent ductus arteriosus, in which there are structural changes to be seen in the lung, is perhaps exactly the same as is found in some types of ventricular septal defect. The reason I ask this question is that we have found in a series of patients with pulmonary hypertension and associated ductus, that closure of the ductus does not necessarily lead to an eventual cure of the hypertension. We have at least 3 patients who are in serious difficulty with pulmonary valve insufficiency, with very large hearts, and we have had 2 patients who have died 6 months or later from complications of pulmonary hypertension.

The second point I would like to discuss is the use of the median sternotomy I am very glad that Dr Lillehei is now using this incision, remembering that Dr Wangensteen advocated it many years ago We have used it for about a year now, in approximately 87 open heart cases, and have found that it is extremely useful and advantageous, particularly in patients who have pulmonary difficulties such as he has described We have not been able to retain the integrity of both pleural spaces in many instances, and always drain the left pleural space as well as the right if it is entered Another drain is always placed near the well fenestrated pericardium to prevent tamponade

It is said that one cannot expose a persistent left superior vena cava through this incision This is untrue, for it is quite easy to bring it into view by retracting the left atrial appendage A large ductus may be difficult to manage if there is gross cardiac and pulmonary artery enlargement, but an average ductus may be dissected intrapericardially

DR SIRAK (Closing) —This afternoon you have seen some suggestions for managing patients who already have severe pulmonary hypertension Dr Muller's discussion brings up the other side of the problem—that is, trying to interrupt this process before it reaches such an advanced stage This problem could best be attacked during infancy These very small patients already have varying degrees of vascular changes, but still have large flows Unfortunately, the risk of open heart surgery in this group is still considerable Therefore, it would seem logical to approach this problem using a two stage method

I should like to show an example illustrating this approach This is a child who at the age of 2 months, developed heart failure and had recurrent pneumonia A pulmonary "tuck" was performed at that time (1955) He did very well until 26 months of age when he began getting cyanotic and had a marked decrease in his activity tolerance Although he had marked clubbing and cyanosis, he had gained in weight from 7 pounds (at the time of the first stage "tuck") to 32 pounds at the time of the second stage open heart procedure (slide) This is the appearance of the anatomy at the time of the open heart operation for repair of the "tuck" and closure of the septal defect (slide) Not shown here is the enormous amount of scar tissue which was present in the bed of the "tuck" area This precluded dissecting out the pulmonary artery I might add that there were very few adhesions in the pericardium After closing the interventricular septal defect, a probe was passed via the right ventricular incision up through the constricted area of the pulmonary artery The artery was then incised from the valve to its bifurcation, demonstrating a very narrow lumen (3 mm) through the "tuck" area A piece of aortic homograft was then sewn to the edges of the opened stenotic area to form a new roof, thereby restoring full patency to the pulmonary artery (slide) I think that the aortic homograft probably will do very well in such a low pressure area and that the diameter is adequate to carry him through adulthood

(slide) This is the cardiac catheterization done just before the pulmonary "tuck" He had a moderate amount of pulmonary hypertension and the biopsy showed moderate vascular changes You will note that the cardiac catheterization done just before the second operation for removal of the "tuck' and closure of the septal defect shows pronounced right ventricular hypertension with a gradient across the "tuck" area The peripheral arterial saturation indicates how markedly cyanotic he had become The last catheterization, performed 2 months after removal of the "tuck" and closure of the defect, shows obliteration of the shunt and normal pressure and saturation values in the right ventricle and pulmonary artery (slide) This is a picture of the child 4 months after the definitive procedure

I should like to ask Dr Lillehei what kind of respirator he uses for complete control of respiration Also, what is the size of the perforations in the Ivalon patch? He mentioned that he is now using the median sternotomy exclusively We have also found this to be a very suitable exposure for all congenital lesions except those associated with a patent ductus

The question is raised whether, in employing a first stage aort [illegible] ary [illegible] as we have advocated, the lungs might be further damaged by the [illegible] of [illegible] left-to-right shunt. I do not believe that this is a problem because flow is reduced through the tubular graft and, furthermore, it is left in place for only a few months. Dr. Lillehei has advocated, in his paper, creating a shunt from the pulmonary artery to the left atrium in order to divert pressure away from the pulmonary arterial bed. By doing this, a tremendous flow-gradient would be established, thus inducing a large bleed-off from the pulmonary artery. I should like to ask Dr. Lillehei whether this might not seriously compromise pulmonary perfusion. The work of the left side of the heart would also be increased.

I would like to thank the discussers, my sponsor, and the Association for the privilege of the floor.

DR. C. WALTON LILLEHEI, Minneapolis, Minn.—This discussion was not returned.—EDITOR.

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Original Communications

CRITERIA OF THYMIC CANCER AND CLINICAL CORRELATIONS OF THYMIC TUMORS

George D Andritsakis, M D, and Sheldon C Sommers, M D, Boston, Mass*

PROBABLY no neoplasms have given pathologists more difficulty in subclassification than thymomas Whether any mediastinal tumor that is malignant can be recognized as of thymic origin is an unsettled question wreathed in controversy The confused and incomplete status of our present knowledge concerning thymic physiology and disease is well known Four important clinical syndromes sometimes accompanied by thymic tumors, i e, agammaglobulinemia, Cushing's syndrome, myasthenia gravis, and refractory anemia, have recently aroused more general interest

In modern pathologic classification, it appears desirable to supersede the primitive inclusive term thymoma Until thyroid surgery became commonplace, the name struma referred similarly to various thyroid and other cervical masses now better understood and classified more definitely In the present clinicopathologic study, the morphologic aspects of thymic tumors that indicated cancerous behavior or suggested the presence of an accompanying clinical syndrome are of primary interest Secondarily classification of thymic tumors and clinicopathologic correlations are considered

Salient events in the history of thymic tumor pathology are listed in Table I Articles reporting small series are too numerous to be cited separately

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From the Departments of Pathology Massachusetts Memorial Hospitals and Boston University School of Medicine Boston Mass

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*Present address Veterans Administration Hospital Surmount N Y

TABLE I. HISTORICAL EVENTS IN THYMIC TUMOR PATHOLOGY

Grandhomme,[18] 1900	Term thymoma introduced
Weigert,[40] 1901	Case report of thymic tumor with myasthenia gravis
Bell,[1] 1917	Eighty-four thymic tumors reported, 11 with myasthenia
Ewing,[15] 1928	Thymic tumors classified as (1) lymphosarcoma or thymoma, (2) carcinoma of reticulum cells
Leyton, et al.,[24] 1931	Thymic tumors in 2 cases of Cushing's syndrome reported
Davidsohn,[11] 1941	Thymic tumor and aregenerative anemia described
Lowenhaupt,[25] 1948	Embryologic classification of thymic tumors proposed
Good,[17] 1954	Thymic tumor with agammaglobulinemia reported

MATERIAL

In this study, fifty tumors considered to be of thymic origin were reexamined histologically and the clinical histories were reviewed. In addition to material from Massachusetts Memorial Hospitals, cases were also obtained through the courtesy of Dr. James A. Graham, St. Elizabeth's Hospital, Dr. William A. Meissner, New England Deaconess Hospital, Dr. Stanley L. Robbins, Boston City Hospital, and Dr. Caesar Tedeschi, Veterans Administration Hospital, Boston. Nine tumors were autopsy specimens, thirty-three were surgically resected from the anterior mediastinum, and eight were represented only by biopsies. Four of the latter were obtained during exploratory thoracotomy. Three were obtained through neck incisions in patients with clinical diagnoses of primary thyroid disease and retrosternal extension. The last biopsy specimen was obtained from a metastatic scalp nodule and the primary mediastinal lesion was not examined.

Seven of the autopsied cases had had advanced symptoms attributed to an expanding mass in the anterior superior mediastinum. Two of the patients died suddenly following administration of Dilaudid and Pentothal, respectively, while x-ray therapy apparently had accelerated the death of 2 others. One autopsied patient with myasthenia gravis died without surgical intervention. In the remaining case, the tumor was an accidental postmortem finding in a patient whose death was ascribed to infestation with *Strongyloides stercoralis.*

PATHOLOGY

A diagnostic classification of thymic neoplasms must take into account three major tissue components of the thymus: (1) thymic parenchymal reticulum, believed to be of entodermal epithelial origin; (2) lymphocytes; and (3) connective tissues, especially fat. The four most recently published English and American detailed subclassifications of thymic tumors, those of Lowenhaupt,[25] Effler and McCormack,[12] Lattes and Jonas,[23] and Thomson and Thackray,[38] have many more similarities in their terminology than differences, considering possible chance variations in the types of case material available. In the present series, composite descriptive terms already proposed in these or other reports are applied to several of the thymic neoplasms, with the designation of adenoma or carcinoma added in accordance with their benign or malignant pathologic characteristics.

Criteria of thymic cancer that have proved applicable to other tissues are microscopic anaplasia, and invasion, either gross or microscopic. The outer fibrous thymic tumor capsule may be found infiltrated or broken by neoplastic outgrowths, and this aggressive behavior indicates a locally malignant change. In fact, most thymic cancers are adenomas with capsular penetration and local tissue invasion, similar to the thyroid adenomas with capsular invasion, adamantinomas or cylindromas in their growth behavior. A few thymic carcinomas have implantation or embolic metastases, mostly within but occasionally outside the *thorax. Liver and cervical lymph nodes are apparently the most* common sites of distant metastasis.

When a mass lying in the usual anatomic position of thymus has a microscopic pattern of epithelial reticulum mingled with lymphocytes and trabeculae reminiscent of thymus, and the patient has no other evident neoplasm elsewhere, a diagnosis of thymic neoplasm is warranted. Such diagnosis need not rest mainly on excluding other possible neoplasms, but rather upon certain positive criteria considered below.

A *Epithelial Neoplasms*.—In view of the common embryonic origin of the thymus, thyroid, parathyroid, and salivary glands from branchial pouches,[5] thymic epithelial neoplasms may logically be termed adenoma or carcinoma. Likewise, the difficulties that are encountered in the subclassification of thymic neoplasms and in the accurate assessment of their possible cancerous behavior are reminiscent of those encountered with neoplasms of the embryologically related *thyroid and salivary glands. About two thirds of the tumors in this* series were adenomas or carcinomas of the thymus, on microscopic examination subclassified as undifferentiated, reticular, trabecular, epidermoid, glandular, or adenoacanthomatous (Table II).

TABLE II. PATHOLOGIC DIAGNOSES OF 50 THYMIC TUMORS

TYPE AND TISSUE	ADENOMA	CARCINOMA	TOTAL
A Epithelial			
1 Undifferentiated	2	2	4
2 Reticular			
a Spindle cell	12	2	14
b Clear cell	2	4	6
3 Trabecular	3	3	6
4 Epidermoid	1	0	1
5 Glandular	0	2	2
6 Adenoacanthomatous	1	0	1
	BENIGN	MALIGNANT	TOTAL
B Lymphoid	0	2	2
C Embryonic	0	1	1
D Fatty	1	0	1
E Cystic	3	0	3
F Hyperplastic	9		9
Totals	34	16	50

1 *Undifferentiated*. 2 adenomas, 2 carcinomas. The 2 tumors considered to be histologically benign had been biopsied through neck incisions, and no data were available as to their gross size or the clinical outcome of the cases.

Microscopically there were masses of large uniform primitive cells, which had an epithelial appearance and which formed linear patterns brought out by reticulum stains (Fig. 1). Invasion was not demonstrated.

One of the 2 undifferentiated carcinomas filled the anterior mediastinum from apex to diaphragm with pink, moist, gelatinous, friable tissue. It had involved the left parietal and visceral pleurae, with microscopic intrapulmonary and mediastinal lymph node metastases and a metastatic nodule in the liver at autopsy. The other carcinoma also involved both the pleura and pericardium. After excision it weighed 685 grams and measured 15 by 8 cm. On section, it was partly fluctuant, variegated gray, red, yellow, and partly necrotic. Microscopically, both tumors were similar. The undifferentiated carcinoma cells were large and eosinophilic with numerous mitoses and prominent nucleoli. Rare spindle cells and abortive concentric laminations of tumor cells simulated malformed Hassall's corpuscles. There was invasion of the dense fibrous stroma and blood vessel walls, with hemorrhage accompanying the latter (Fig. 2).

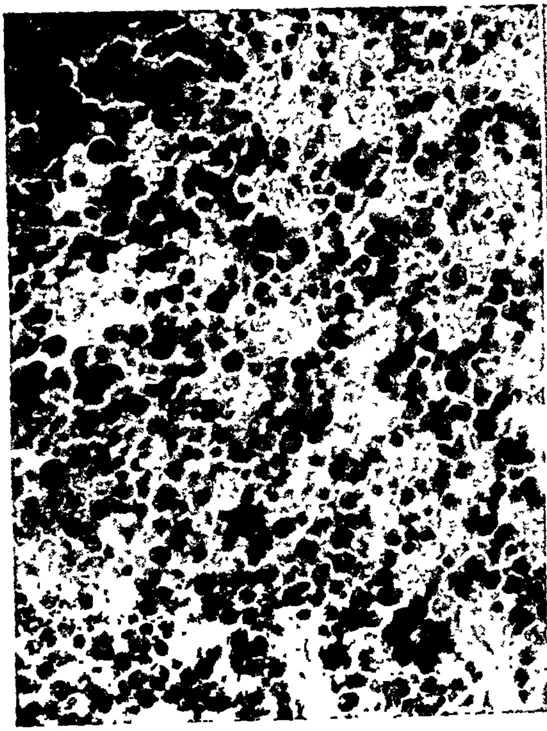

Fig. 1.

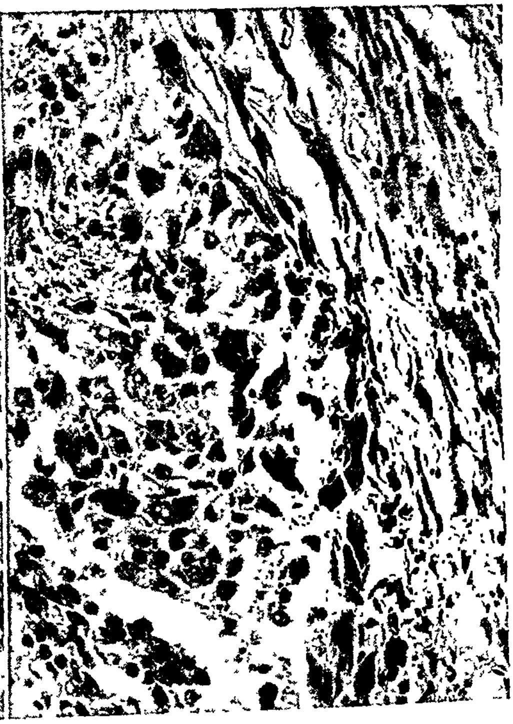

Fig. 2.

Fig. 1.—Portion of undifferentiated thymic adenoma, with pattern of large pale epithelial reticulum cells and smaller rounded lymphocytes This type of tumor is sometimes called lymphoepithelioma. (Hematoxylin and eosin; ×500.)

Fig. 2.—Metastatic undifferentiated thymic carcinoma in liver. Abundant eosinophilic cytoplasm and variable nuclei of tumor cells are shown. (Hematoxylin and eosin; ×125.)

2. *Reticular:* 14 adenomas, 6 carcinomas. Two subtypes were recognized, (a) spindle cell and (b) clear cell.

a. The reticular spindle cell adenoma, referred to as reticular perithelioma by Pope and Osgood[30] and as lymphangio-endothelial by Hubbell and Liebow,[19] is the most common and best known thymoma The 12 spindle cell tumors weighed from 75 to 320 grams, averaging 144 grams in 10 cases, and measured from 7 by 5 by 4 cm. to 13 by 9 by 6 cm. Spindle cell adenomas occurred in every clinical group except Cushing's syndrome. They were well encapsulated, firm, and the cut surfaces were usually shining pink to yellow-tan and moist, with gray fibrous trabeculations projecting into the solid tumor, producing lobulations (Fig. 3).

Microscopically, as frequently described previously, the oval, spindly epithelial cells were closely packed in cords and sheets with some perivascular

Fig 3—Typical gross appearance of sectioned thymic spindle cell adenoma, weighing 320 grams, removed from a 57-year-old man

whorling Rare Hassall's bodies were seen. There was local palisading around vessels, and simulation of rosettes, as well as growth patterns imitative of certain meningiomas (Fig 4) The epithelial masses were pale or brightly eosinophilic and often formed lobular masses between which sheets of lymphocytes were seen. The latter were also interspersed among the reticular cells Anaplasia and mitoses were usually absent. Dilated lymphatics, foci of phagocytosis of hemosiderin, and areas of hyalinization of the collagenous stroma were frequent.

There were 2 reticular spindle cell carcinomas, and they were larger than the adenomas; one weighed 310 grams and measured 14 by 11 by 10 cm. The second encircled the great vessels and invaded the pericardium It was not resected and hence was not weighed or measured. The resected tumor appeared encapsulated, but histologically it appeared anaplastic and invasive and showed a peculiar hyaline droplet degeneration between the cells. Lymph node metastases were present, with similar intercellular droplets (Fig. 5).

b. Reticular clear cell adenomas were represented by two tumors, weighing 75 and 120 grams. The latter was associated with myasthenia gravis. Grossly, they resembled other thymic adenomas, but microscopically the epithelial reticulum was composed of masses of large polygonal cells, many with watery cytoplasm, oval nuclei, and rather coarse nuclear chromatin (Fig. 6). There were 4 reticular clear cell carcinomas included, weighing from 65 to 130 grams. They appeared to be partly encapsulated (Fig. 8), but microscopically invaded the surrounding fibrous stroma, and in 2 of 4 cases the adjacent chest wall or lymph nodes (Fig. 7).

3. *Trabecular:* 3 adenomas, 3 carcinomas. This variety, also called adamantinomatous or cribriform, histologically simulates some neoplasms of other branchial pouch derivatives. Two trabecular adenomas were examined at autopsy. One, occurring in a case of myasthenia gravis, measured 6 by 5 by 3 cm.; the other was 16 cm. in diameter and weighed 320 grams. They were pink, glistening, and lobulated. Microscopically, the epithelial reticulum grew in cords and nodules of palisaded cells, regularly arranged in trabeculae and in focal areas lined up along lymphatic spaces (Fig. 9). The third trabecular adenoma was only biopsied.

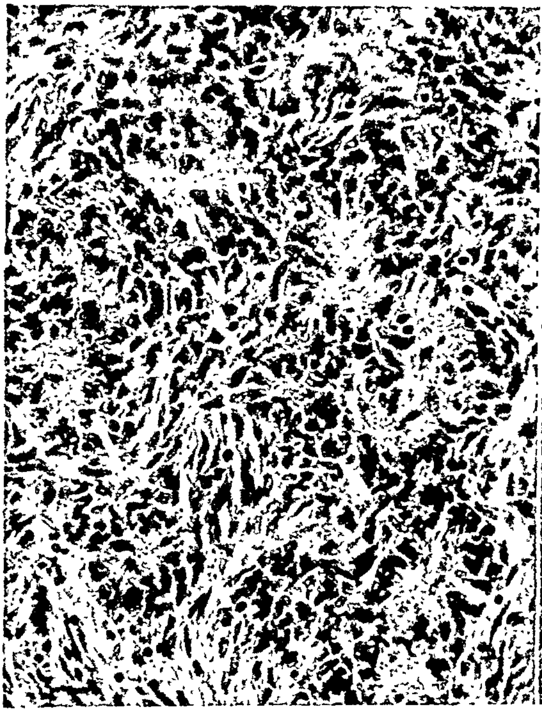

Fig. 4.

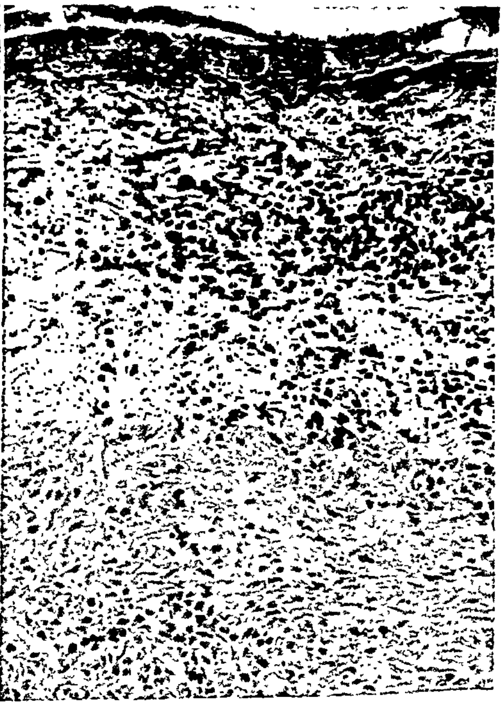

Fig. 5.

Fig. 4.—Rosette-like growth pattern of reticular spindle cell adenoma and elongated shapes of epithelial reticulum cells are evident. (Hematoxylin and eosin; ×125.)

Fig. 5.—Lymph node metastasis of a reticular spindle cell carcinoma has locally replaced most of the lymphatic tissue, but the capsule remains identifiable at the top. (Hematoxylin and eosin; ×120.)

All three trabecular carcinomas produced pressure symptoms, surrounded the great vessels and trachea, and invaded the pleura and pericardium. Two

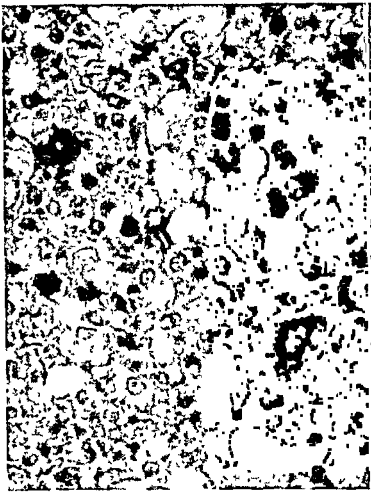

Fig. 6

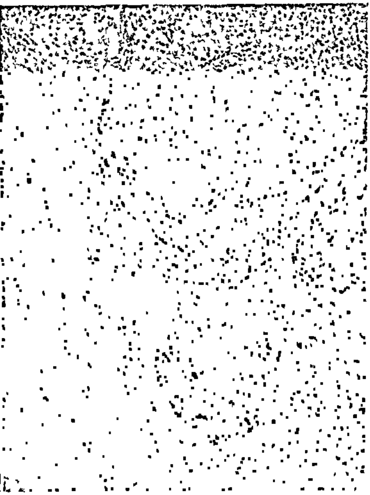

Fig. 7.

Fig. 6.—Clear reticulum cells from a thymic adenoma are shown. The two dark larger cells contain PAS-positive cytoplasmic granules. (PAS-aldehyde fuchsin-light green; ×600.)

Fig. 7.—Invasion of mediastinal connective tissue by masses of thymic carcinoma, which also infiltrated adjacent lung. (Hematoxylin and eosin, ×60.)

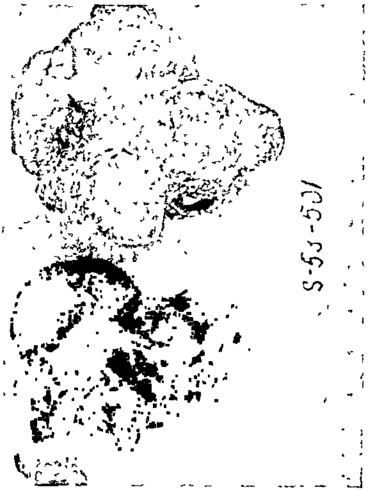

Fig. 8.—Grossly poorly demarcated and encapsulated thymic clear cell carcinoma from a 56-year-old man. (From the same case as Fig. 7.)

b. Reticular clear cell adenomas were represented by two tumors, weighing 75 and 120 grams. The latter was associated with myasthenia gravis Grossly, they resembled other thymic adenomas, but microscopically the epithelial reticulum was composed of masses of large polygonal cells, many with watery cytoplasm, oval nuclei, and rather coarse nuclear chromatin (Fig 6). There were 4 reticular clear cell carcinomas included, weighing from 65 to 130 grams. They appeared to be *partly encapsulated* (Fig. 8), but microscopically invaded the surrounding fibrous stroma, and in 2 of 4 cases the adjacent chest wall or lymph nodes (Fig. 7).

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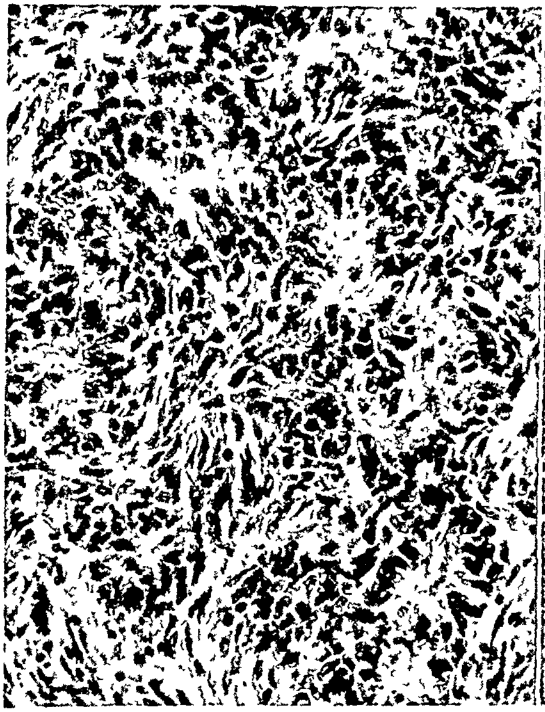

Fig 4

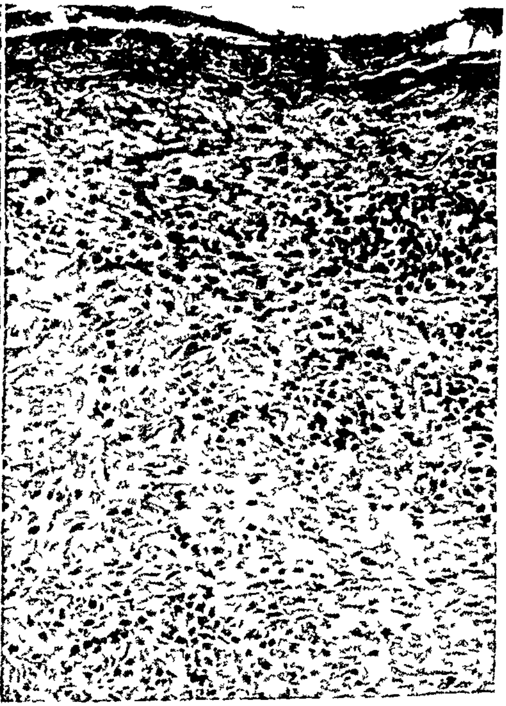

Fig 5.

Fig 4 —Rosette-like growth pattern of reticular spindle cell adenoma and elongated shapes of epithelial reticulum cells are evident (Hematoxylin and eosin, ×125)

Fig 5 —Lymph node metastasis of a reticular spindle cell carcinoma has locally replaced most of the lymphatic tissue but the capsule remains identifiable at the top (Hematoxylin and eosin, ×120.)

All three trabecular carcinomas produced pressure symptoms, surrounded the great vessels and trachea, and invaded the pleura and pericardium Two

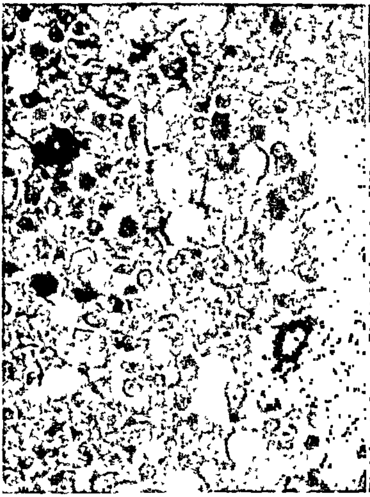

Fig. 6

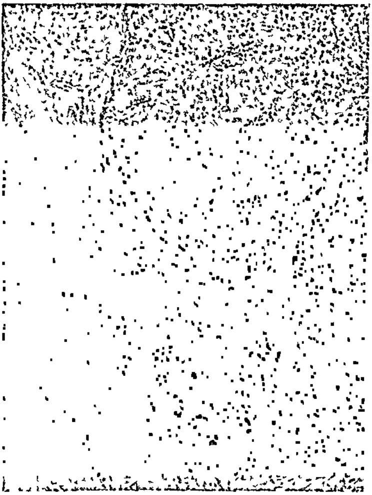

Fig. 7.

Fig. 6.—Clear reticulum cells from a thymic adenoma are shown. The two dark larger cells contain PAS-positive cytoplasmic granules (PAS-aldehyde fuchsin-light green; ×600.)

Fig. 7—Invasion of mediastinal connective tissue by masses of thymic carcinoma, which also infiltrated adjacent lung. (Hematoxylin and eosin, ×60.)

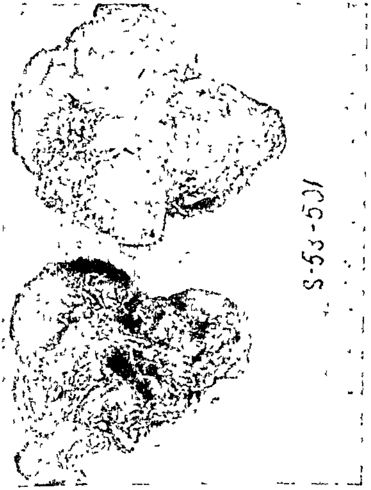

Fig. 8—Grossly poorly demarcated and encapsulated thymic clear cell carcinoma from a 56-year-old man (From the same case as Fig. 7.)

cases had implants on the posterior thoracic wall and diaphragm. Microscopically, there were characteristic tortuous ribbon-like cords of epithelium with nuclear anaplasia, reminiscent of some ameloblastic and salivary carcinomas (Fig. 10).

4. *Epidermoid:* 1 adenoma. Several thymic tumors had squamous foci, either as sheet-like masses or concentric nodules in 5 cases (Fig. 11), or with recognizable Hassall's bodies in 7 of the total 37 solid neoplasms In addition, some degenerative cysts had squamous linings of epithelial reticulum cells. These cells were squamous-like but did not show all the morphologic details of epidermal squamous cells. One benign asymptomatic adenoma, 10 cm. in diameter, was found composed predominantly of epidermoid cells, with abundant eosinophilic cytoplasm and Hassall's corpuscles. Pure epidermoid carcinoma of thymus has been reported.[16]

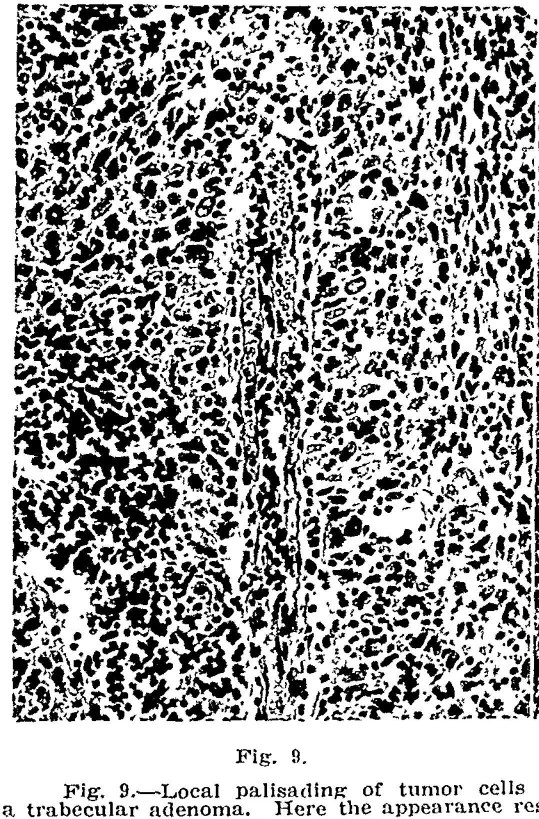

Fig. 9.

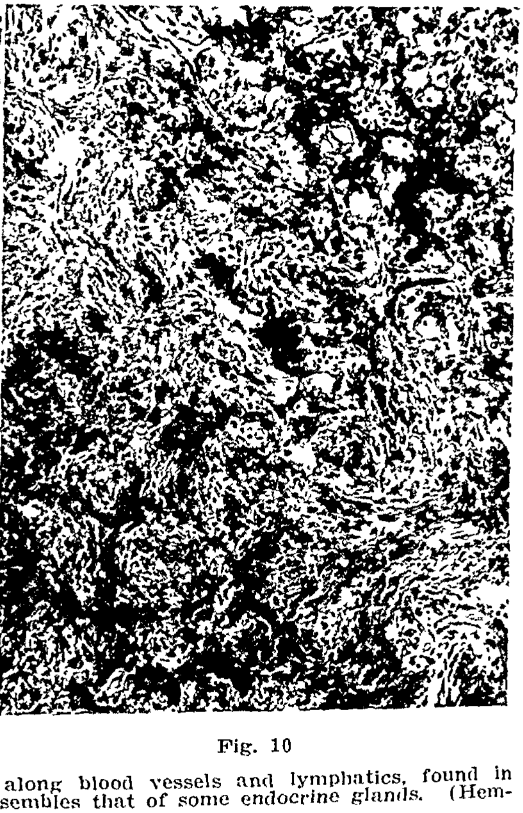

Fig. 10

Fig. 9.—Local palisading of tumor cells along blood vessels and lymphatics, found in a trabecular adenoma. Here the appearance resembles that of some endocrine glands. (Hematoxylin and eosin; ×200.)

Fig. 10.—Trabecular carcinoma with cordlike growth pattern and invasion of fibrous connective tissue. (Phosphotungstic acid-hematoxylin; ×80.)

Granulomatous thymoma or so-called Hodgkin's variant of thymoma is a separate subtype of tumor listed in several other classifications.[26] In the present series, granulomatous-appearing foci of epithelial reticulum cells were observed locally in one case each of clear cell adenoma, spindle cell carcinoma, clear cell carcinoma, and trabecular carcinoma. Such multinucleated giant cells occurred in otherwise typical thymic neoplasms chiefly in regions of marked degeneration and fibrosis, as postirradiation, or in the invasive or metastatic carcinomatous portions.[14]

The granulomatous or giant cell foci were usually characterized by large mononuclear or multinucleated cells closely simulating the Reed-Sternberg cells of Hodgkin's disease, particularly in hematoxylin and eosin preparations. Nucleoli were prominent and the nuclear chromatin scanty. At times, concentric whorls of similar cells had a nuclear elongation, indicative of their thymic origin, and not seen in lymphomatous reticulum cells.[34, 37] The periodic acid-Schiff (PAS)[21] or Gomori aldehyde fuchsin methods stained coarse granules, respectively, red and purple in the epithelial giant cell cytoplasm (Fig. 12). Genuine Reed-Sternberg cells contained no cytoplasmic [illegible] les

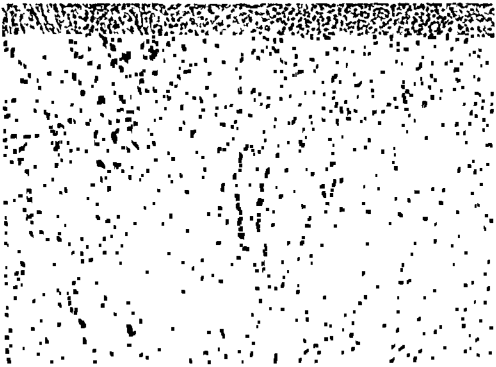

Fig 11.—Focal epidermoid growth pattern of thymic carcinoma, with invasion of lung, surrounding the small bronchi in the center. Elsewhere this thymic carcinoma had a reticular pattern (Hematoxylin and eosin, ×125.)

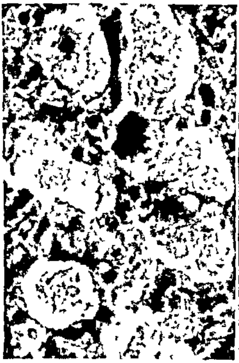

Fig 12

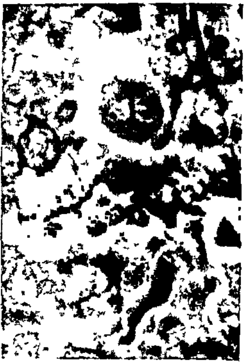

Fig. 13

Fig. 12.—Special stain of giant cells from granulomatous focus of thymic carcinoma, demonstrating the cytoplasmic granulations characteristically found. (PAS-aldehyde fuchsin-light green, ×750.)

Fig 13.—Same stain of specimen of Hodgkin's disease, with Reed-Sternberg cell, showing no cytoplasmic granules (PAS-aldehyde fuchsin-light green, ×750.)

that were stained by these methods (Fig. 13). Differential staining may warrant a wider application in future investigations of Hodgkin's disease, particularly as to its imputed thymic origin.

5. *Glandular:* 2 carcinomas. The benign adenoma of pure glandular pattern is unknown, but thymic adenocarcinoma has a significant status because of its peculiar relation to Cushing's syndrome. This combination has been described in 10 reported cases.[8, 9, 37]

One comparable case of the syndrome, previously reported,[37] had a 1,898 gram thymic adenocarcinoma with a histologic ribbon-like epithelial pattern excised. It had invaded the left lung. The patient did not survive operation, and at autopsy there was an embolic metastasis of adenocarcinoma to a mediastinal lymph node. The other case was that of a 63-year-old, asymptomatic man without endocrine disease. He had a 135 gram, 8 by 6 by 5 cm., homogeneous, pink thymic adenocarcinoma resected. There was lymphatic invasion and metastases to 1 of 10 regional lymph nodes. Microscopically, the tumor was in part composed of cuboidal epithelium and somewhat resembled mammary carcinoma (Fig. 14).

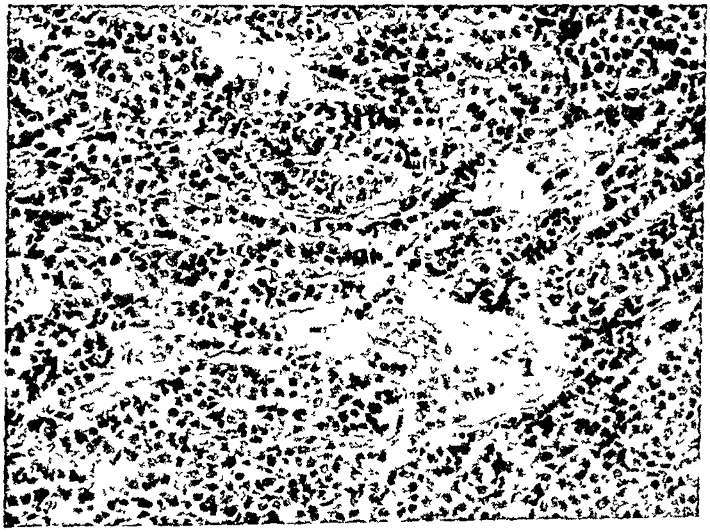

Fig. 14.—Thymic adenocarcinoma, without apparent endocrine correlations, growing in cords of cuboidal cells, with hyalinized stroma. (Hematoxylin and eosin; ×125.)

6. *Adenoacanthomatous:* 1 adenoma. This tumor measured 8 by 5 by 1 cm. and produced pressure symptoms in a 72-year-old man. It was adherent to the aorta and pericardium at the cardiac base, and was locally calcified. Microscopically, there were glandular, papillary, and adamantinomatous regions, as well as epithelial cords, keratinized sheets and whorls, with partly formed Hassall's corpuscles. No invasion was observed.

Some thymic adenomas and carcinomas showed evident transitions between, and intermingling of, the reticular, trabecular, glandular, and epidermoid types of differentiation. Foci of reticular spindle or clear cells occurred in some neoplasms that were elsewhere chiefly trabecular. This variability of pattern at times made classification difficult, a problem which is also encountered in salivary gland neoplasms. The multiform growth patterns of thymic tumors may reflect the complex processes observed in its embryogenesis.[25]

B. *Lymphomas.*—Two tumors are included. One was discovered in the chest x-ray film of a 77-year-old woman. On operative exploration, a large mass measuring 15 by 15 cm. was found in the anterior mediastinum. The tumor was solid with many fungating excrescences around the large vessels. The other case, in a 9-year-old girl, was recognized at autopsy. The entire mediastinum was filled with tumor. Her death was ascribed to pneumonia secondary to bilateral compression of the major bronchi by tumor.

The neoplasm in the adult case was composed of rather large immature lymphoid cells with spherical or notched nuclei, classified as lymphosarcoma. In the child, mature lymphocytes predominated, and the tumor was considered a malignant lymphocytoma. Both neoplasms infiltrated and penetrated the fibrous thymic capsule, vessel walls and trabecular stroma in the manner characteristic of malignant lymphomas. In neither case was any lymphoma found elsewhere in the body.

C. *Embryonal Carcinoma.*—One case was so diagnosed. The patient had an anterior mediastinal tumor, clinically regarded as Hodgkin's disease and treated with nitrogen mustard. Tissue was not obtained from the primary tumor, but before he died a metastatic lesion on the scalp was biopsied. Microscopically, the appearance was comparable to a poorly differentiated dysgerminoma or testicular carcinoma, without any teratomatous features or lymphoid stroma. It was compatible with a mediastinal embryoma of the "seminomatous" type reported to develop in the thymus.[29, 32]

D. *Thymolipoma.*—The one case found was asymptomatic; the tumor was discovered in a routine roentgenogram of the chest. It measured 11 by 7 cm., weighed 54 grams, and had the consistency and appearance of an ordinary lipoma. It was loosely adherent to the mediastinal structures, and microscopically was wholly composed of adult fat, aside from fibrous trabeculae suggesting thymus.[39]

E. *Cysts.*—Three cystic tumors are included. One was located in the neck, and 2 in the mediastinum. The cyst in the neck measured 4.5 by 4.5 by 0.2 cm. and was loosely adherent to the surrounding tissue. The cysts located in the anterior mediastinum measured 11 by 9 by 5 cm. and 9 cm. in diameter, with walls averaging 0.5 cm. in thickness. They were loosely adherent to the surrounding tissues and contained thin viscid fluid.

Microscopically, all 3 cysts had thymic tissue in their walls. The cervical and one of the mediastinal cysts were lined by epithelium like that found in branchial cleft cysts,[41] squamous in the cervical and mixed columnar, mucus-producing and ciliated in the mediastinal cyst. The other cyst was lined by mesothelium.[10] A cystic thymic choristoma has been described.[6]

F. *Hyperplasias.*—Nine tumors were included, which some pathologists would prefer to consider lymphoepitheliomatous thymomas. The largest weighed 550 grams and had the appearance of a tremendously enlarged thymus, with a longitudinal fibrous furrow dividing the mass into two lobes. The smallest tumor measured 9 by 7 by 4 cm. The average tumor was 3.5 by 1.8 cm. and weighed 250 grams (Fig. 15). All had a well-formed fibrous capsule

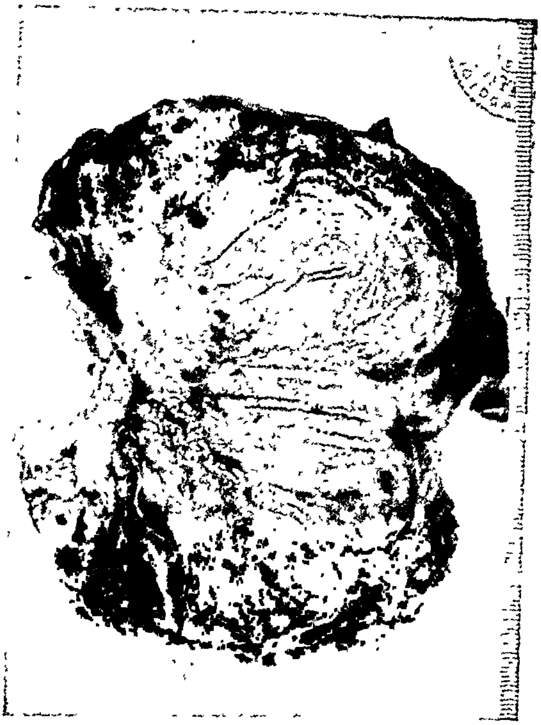

Fig. 15.—Thymic hyperplasia, with shape and appearance of greatly enlarged thymus, measuring 10.5 × 9.5 × 7 cm.

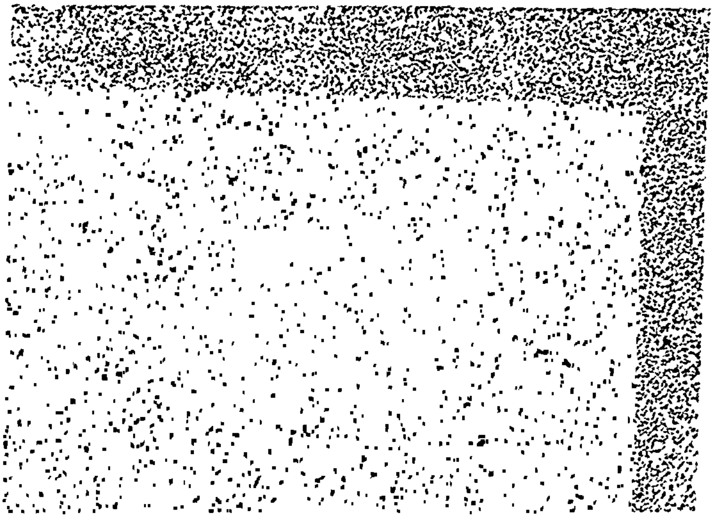

Fig 16.—Simulation of germinal center of lymphatic tissue in a thymic hyperplasia accompanying myasthenia gravis. (Hematoxylin and eosin; ×80.)

that sent projections into the tumor dividing it into lobules. Cut surfaces were of pink or yellowish-pink color. Two tumors associated with myasthenia gravis contained small cysts filled with a gelatinous semisolid material. The rest were homogeneous. Hemorrhages were frequently present. Microscopically, no definite cortex or medulla was distinguishable; instead there was a generalized overgrowth of all thymic constituents except for Hassall's corpuscles, which were relatively few Sometimes the thymic reticulum appeared vacuolated and formed rounded, lightly stained foci resembling germinal centers in lymphatic tissue (Fig 16) No homogeneous or localized proliferations were seen that could be termed neoplastic In these 9 cases, there was no evidence of cancer and it is not clear that either major thymic component was neoplastic Similar cases were included in the group designated hyperplasia by Bivan, McDonald, and Clagett[7]

CLINICAL DATA

From data available in the clinical records 5 distinct clinical groups were distinguished (Table III) One case could not be included in the clinical survey because of insufficient information

TABLE III CLINICOPATHOLOGIC CORRELATIONS OF 50 THYMIC TUMORS

	CLINICAL GROUP					
	PRESSURE AND MISC SYMPTOMS*		ASYMPTOMATIC		MYASTHENIA GRAVIS	
A Adenoma and Carcinoma	*Ad*	*Ca*	*Ad*	*Ca*	*Ad*	*Ca*
1 Undifferentiated	2	2	0	0	0	0
2 Reticular						
a Spindle cell	5	1	5	1	2	0
b Clear cell	1	1	0	2	1	1
3 Trabecular	1	2	1	1	1	0
4 Epidermoid	0	0	1	0	0	0
5 Glandular	0	1	0	1	0	0
6 Adenomatous	1	0	0	0	0	0
B Lymphoma		1		1	0	
C Embryoma		1	0		0	
D Lipoma	0		1		0	
E Cysts	1		2		0	
F Hyperplasia	3		4		2	
Total number of cases	23		20		7	

*Includes 2 cases of refractory anemia and 1 case of Cushing's syndrome

1 *Pressure Symptoms*—20 cases Usually there were indications of an expanding mass in the anterior superior mediastinum These symptoms varied from the mildest anterior chest wall discomfort, pain, and cough to a marked venous distention of the neck and upper chest wall, with edema of the face and neck, cyanosis, dyspnea, and orthopnea Hemoptysis and dysphagia were each present in three instances Weight loss was marked in the more advanced cases Three patients operated on prior to 1939 had tumor extensions into the suprasternal region, clinically originally interpreted in two instances as colloid goiter and in the third as a carcinoma of the thyroid with retrosternal extension One patient had a swelling in the lateral aspect of the neck like a typical branchial cleft cyst The youngest patient in this group was 7 and the oldest 72 years old Seven patients died without surgical intervention

In all of the autopsied cases, there was invasion of one or more of the adjacent organs such as pericardium and pleura, as well as involvement of the large vessels of the superior mediastinum As shown in Table III, there were 9 malignant thymic neoplasms among the 20 with pressure symptoms

Most of the total thymic cancers in this series were found in this clinical group, and 2 of the 4 cases with lymph node metastases had pressure symptoms The other 2 patients were asymptomatic.

2. *Asymptomatic.*—20 cases. These tumors were discovered either accidentally during a complete medical investigation or in a survey x-ray film One tumor was found at the autopsy of a patient who died from an unrelated cause. Two were cysts, both loosely adherent to the surrounding tissues, the larger weighing 275 grams and measuring 11 by 9 by 6.5 cm. All but two of the solid neoplasms were well encapsulated and without invasion. They were completely excised. The largest measured 13 by 9 by 6 cm. and weighed 320 grams, and the smallest measured 6 by 5 by 4 cm. and weighed 65 grams

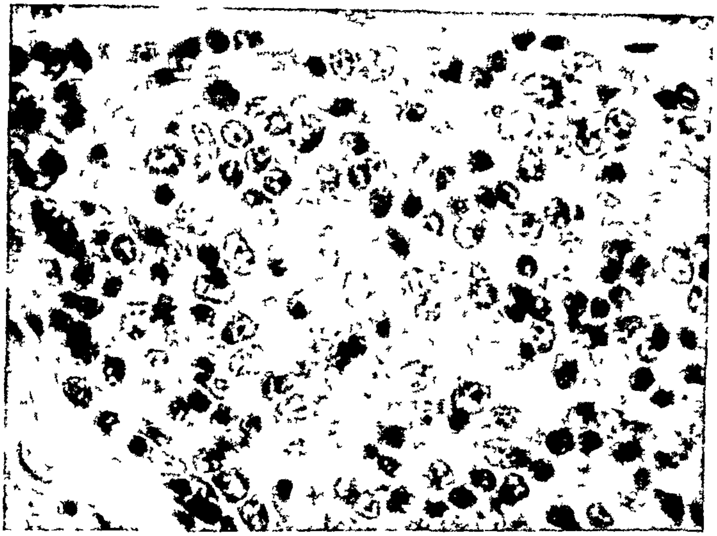

Fig. 17—Part of a reticular thymic adenoma in a case of aregenerative anemia The peculiar block-like nuclear chromatin in the smaller rounded lymphoid cells is illustrated, in contrast to the appearance of Fig 1 (Hematoxylin and eosin, ×500)

Of the 2 tumors that were not sharply demarcated, one was a relatively small mass measuring 5 by 4 by 3 cm. that had invaded the hilum of the left lung. It was excised together with the lung. The second measured 15 by 15 cm, had invaded the pleura, the pericardium and surrounded the great vessel Only a biopsy was obtained. This latter tumor had been visualized first in a chest roentgenogram 14 years prior to surgical exploration. The youngest patient in the group was 20 years old and the oldest 63. Five of the 20 cases were diagnosed pathologically as thymic cancers

3. *Myasthenia Gravis.*—7 cases. The average age was 40 years, ranging from 29 to 50 years. There were 4 women and 3 men. The average duration of symptoms prior to operation was 6 months, varying from 1 to 16 months. Pathologic diagnoses were thymic hyperplasia in 2 cases, reticular cell adenoma in 3, reticular carcinoma with capsular invasion in one, and trabecular adenoma in 1 case.

All 7 thymic tumors with myasthenia gravis, whether of hyperplastic or neoplastic type, contained abundant foamy or vacuolated reticulum cells resembling clasmatocytes, either scattered or in nodules in the thymus suggesting lymph node germinal centers.[20] This histologic feature was considered most suggestive of myasthenia,[1, 2, 35] although 3 other cases not associated with any neuromuscular disease also had structures present in thymic tumors resembling germinal centers. Six patients had the tumors excised, and one died before any surgical intervention, 6 weeks after the onset of symptoms. In one patient, myasthenia first developed following excision of the tumor.[13, 27] Another patient had a multi-endocrine disorder characterized by hypopituitarism with secondary hypogonadism and adrenal hypofunction. Myasthenia developed during endocrine treatment.

Six of the tumors were well encapsulated and offered no technical difficulty to the surgeon. Only one had invaded the pleura and surrounded the great vessels. The largest tumor weighed 140 grams and measured 9 by 6 by 3.5 cm., the smallest weighed 25 grams and measured 2 cm. in diameter.

4. *Aregenerative Anemia.*—2 cases. These cases have been previously reported.[33, 37] Both tumors were well encapsulated, measuring 8 by 6 cm. and 10 by 9 by 5 cm., the weight of the latter being 270 grams. Both were surgically excised and classified pathologically as reticular spindle cell adenomas. The associated lymphocytes were peculiar because of an abnormal block-like appearance of their nuclear chromatin, and similar abnormal "lymphoid" cells were present in the bone marrow biopsies that were completely devoid of erythropoiesis (see Fig. 17).[3] One woman later developed agammaglobulinemia.[22]

5. *Cushing's Syndrome.*—1 case. A 32-year-old man was subjected to thoracotomy and died during surgery. The tumor was found to be a thymic adenocarcinoma which was densely adherent to, and encircling the innominate veins, and had also invaded the pericardium and the hilum of the left lung.[37]

DISCUSSION

Recent studies of larger numbers of thymic tumors have improved pathologic knowledge concerning classification of these peculiar and challenging neoplasms. The epithelial nature of a majority now seems accepted, as indicated by the terms of previous authors such as adamantinomatous, lymphoepitheliomatous, and cribriform. Acceptance of most thymic neoplasms either as adenomas or carcinomas may encourage a closer correlative comparison with the tumors of other branchial pouch derivatives.

That thymic cancers metastasize only occasionally need not prevent their recognition. Ameloblastomas, basal cell carcinomas, cylindromas, gliomas, certain thyroid tumors like so-called "wuchernde Struma," and malignant meningiomas, among others, are recognized as cancers not likely to metastasize. Local compression, destruction and invasion of mediastinal structures may prove fatal in some thymic cancers before any metastatic deposits become established. Surgical specimens carefully studied may show invasion of attached lung, lymph nodes, and mediastinal connective tissues.

Many mysteries surround the thymus as a possible endocrine gland or a reflector of a hormonal deficiency, such as with adrenal cortical or medullary hypofunction.[31] Lymphocytes apparently are attracted by the epithelial

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THE NATURAL HISTORY OF CARCINOMA OF THE LUNG

George L. Emerson, M.D., Marion S. Emerson, M.D., and
Charles E. Sherwood, M.D., Rochester, N. Y.

In the majority of instances, early diagnosis and ablation of cancer will yield the greatest number of cures. Since the most radical operation practicable is currently used for cancer of the lung, earlier diagnosis should improve the present 3 to 6 per cent cure rate.

Use of clinical diagnostic methods such as bronchoscopy, cytology, scalene biopsy, and thoracotomy have increased in recent years and have helped to make earlier definitive diagnosis. However, a significant change on a roentgenogram of the chest frequently is the first positive finding and often precedes clinical symptoms. The principal objective of this study has been to gain new information about these early changes and, where possible, to observe the alteration in such x-ray shadows with the passage of time. To this end, all roentgenograms obtainable on proved cases of pulmonary cancer have been collected and studied.

METHOD

Over 400 cases of pulmonary cancer seen in this hospital have been reviewed. This report covers 360 proved cases, the majority having been diagnosed within the past 15 years. Records were abstracted and information was solicited from surviving patients, families, physicians, hospitals, and other institutions where radiographs may have been taken. Any past radiographs available were gathered and reviewed in conjunction with later films made at the time of the diagnosis of the patient's carcinoma. All films were studied in joint session by the authors. Where there was any question of the presence of an abnormal shadow, the opinion of two unbiased senior radiologists was obtained.

RESULTS

While the radiographic study of these cases has been the prime aim of the project, certain ancillary statistical information is included for general interest with no further elaboration. Tables I through VI list statistics relating to age, sex, occupation, smoking habits, symptoms, diagnostic methods, and cell type.

From the Departments of Medicine, Radiology, and Surgery, The University of Rochester School of Medicine and Dentistry, Rochester, N. Y.

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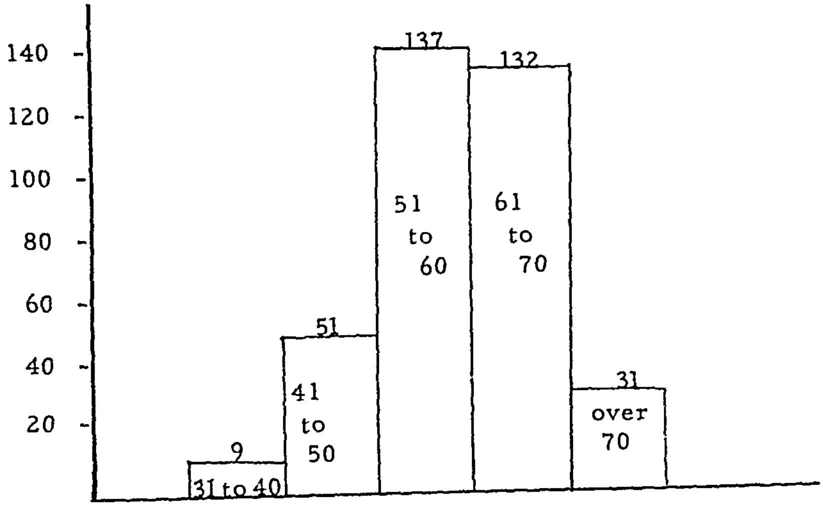
TABLE I. SEX AND AGE DISTRIBUTION IN 360 CASES OF LUNG CANCER

	NUMBER	PER CENT	AVERAGE AGE
Male	313	87	59.4
Female	47	13	56.2
Total	360	100	58.9



Age distribution of patients

TABLE II. OCCUPATIONS IN 360 CASES OF LUNG CANCER*

OCCUPATION	NUMBER	PER CENT
White collar worker	82	22.8
Housewife	37	10.3
Not known	34	9.4
Hazardous dust exposure	29	8.1
Truckdrivers and mechanics	26	7.2
Laborers	18	5.0
Carpenters	17	4.7
Farmers	15	4.2
Machinists	14	3.9
Painters	12	3.3
Railroad yard and engine workers	9	2.5
Restaurant workers	8	2.2
Tailors	8	2.2
Janitors	6	1.7
Plumbers	5	1.4
Pressers	5	1.4
Garbage collectors	4	1.1
Bartenders	3	0.8
Barbers	3	0.8
Gardeners	3	0.8
Laundry workers	3	0.8
Porters	3	0.8
Stationary engineers	3	0.8
Basket weavers	2	0.6
Firemen	2	0.6
Grocers	2	0.6
Policemen	2	0.6
Printers	2	0.6
Miscellaneous (1 each)	5	0.3

*Total figure reflects multiple occupations.

TABLE III SMOKING HABITS IN 360 CASES OF LUNG CANCER

	WOMEN		MEN		TOTAL	
	NO	%	NO	%	NO	%
No information	18	38	129	41	147	41
Nonsmokers	18	38	7	2	25	7
Group A smokers*	6	13	92	30	98	27
Group B smokers†	5	11	85	27	90	25
Total	47	100	313	100	360	100

	MEN EXPOSED TO DUST‡		MEN EXPOSED TO COMBUSTION FUMES		TOTAL FOR SMALLER GROUP PAST 4 YEARS§	
	NO	%	NO	%	NO	%
No information	9	31	6	23	39	24
Nonsmokers	0	—	0	—	12	7
Group A smokers	7	24	4	15	56	35
Group B smokers	13	45	16	62	55	34
Total	29	100	26	100	162	100

*Smokers of less than 1 package per day

†Smokers of 1 package or more per day for 20 plus years

‡For example dusts with a potential for producing pneumoconiosis

§Reflects better recorded information in more recent years

TABLE IV OCCURRENCE OF SYMPTOMS IN 360 CASES OF LUNG CANCER

FIRST SYMPTOM	NO	%	LATER SYMPTOMS	NO	%
1 Cough	194	54	1 Sputum	214	60
2 Chest pain	38	11	2 Chest pain	151	42
3 Weight loss	30	8	3 Hemoptysis	130	36
4 Dyspnea	20	6	4 Dyspnea	109	30
5 No symptoms	19	5	5 Weight loss	89	25
6 Fatigue	17	5	6 Cough	85	23
7 Bone pain	12	3	7 Wheeze	37	10
8 Pleuritic pain	7	2	8 Pleuritic pain	27	8
9 Nerve disorder	7	2	9 Hoarseness	23	6
10 Hemoptysis	5	1	10 Nerve disorder	21	6
11 Hoarseness	4	1			
12 Mass in neck	3	1			
13 Misc (1 each)	4	1			

TABLE V DIAGNOSTIC PROCEDURES IN 360 CASES OF CARCINOMA OF THE LUNG

PROCEDURE	NUMBER	PER CENT OF PROCEDURES	PER CENT OF SERIES
Bronchoscopy			
Total examinations	230	100	64
Abnormal appearance	191	83	53
Positive biopsy	99	43	28
Negative biopsy	39	17	11
Scalene Biopsy			
Total examinations	70	100	19
Positive biopsy	46	66	13
Negative biopsy	24	34	7
Papanicolaou Smear			
Total examinations	84	100	23
Positive	63	75	17
Negative	21	25	6
Thoracotomy			
Total operations	150	100	42
Pneumonectomy	60	40	17
Lobectomy	18	12	5
Nonresectable	72	48	20

TABLE VI. CELL TYPE IN 360 CASES OF CARCINOMA OF THE LUNG

CELL TYPE	MEN	WOMEN	TOTAL	PER CENT
Epidermoid	137	9	146	40
Undifferentiated epidermoid	127	16	143	40
Adenocarcinoma	16	17	33	9
Oat cell	17	0	17	5
Not classified	6	3	9	3
No section (gross appearance; cytology)	10	2	12	3

Table VII is a clinical analysis of 10 patients surviving 5 years or more, an incidence of 2.8 per cent of the total group and 3.1 per cent of the cases seen during the 15-year period in which these survivors were diagnosed.

Table VIII indicates the average interval from the first symptom to clinical diagnosis, to pathologic diagnosis, and to death in varying numbers of patients.

Of major concern in this study is the information tabulated in Tables IX and X. These indicate the average interval elapsing between the earliest radiographic evidence of the individual's cancer and the clinical diagnosis (Table IX) and the pathologic diagnosis (Table X). In each case, this is averaged for four categories: (1) all cases; (2) excluding patients in which the interval between the earliest radiographic evidence and diagnosis was zero; (3) excluding patients in which this interval was less than 3 months; and (4) excluding all cases in which this interval was less than 6 months. Because of the nature of the shadows seen in x-ray studies at the time of diagnosis, it is highly probable that some abnormality would have been present if films had been taken at any point during the 6 months or year prior to diagnosis. Therefore, the more significant is the last group. Rigler and his group have been interested in the duration of pulmonary cancer for some time and have brought out this point.[3, 4]

Radiographic Findings.—As previously stated, the major interest in this project has centered around a study of the early radiographic evidences of carcinoma of the lung. In reviewing all earlier films, changes have been sought which could be correlated with the eventual, more gross evidence, of the neoplasm. The types of change seen and their frequency are recorded in Table XI.

1. *Obstructive pneumonitis:* One of the commonest morphologic manifestations of lung cancer, found in 36 per cent of this series, is the encirclement of, or growth into, a bronchus by the neoplasm. This produces a partial obstruction and consequent poor drainage distally. Radiographically, the tumor itself may not be seen while the secondary changes of obstructive pneumonitis are quite common. The term implies a subacute or chronic infiltration with additional evidence of decreased lung volume locally. An illustration of this is given in Figs. 1-4. The inflammatory process is indicated by the heavy linear infiltration at the left base and the partial atelectasis by the elevated diaphragm.

2. *Parenchymal mass:* Twenty-two per cent of the cases had radiographs revealing the direct shadow produced by the more peripherally situated tumor. Illustrations of this are found in Fig. 5, representing a slowly growing lesion, and in Figs. 6-9, representing a rapidly progressive neoplasm. It will be noted

TABLE VII. CLINICAL ANALYSIS OF 10 CASES OF LUNG CANCER SURVIVING 5 OR MORE YEARS AFTER OPERATION

CASE	SEX	INTERVAL FIRST SYMPTOM TO DIAGNOSIS (MO.)	INTERVAL FIRST X-RAY CHANGE TO DIAGNOSIS	OPERATION	CELL TYPE	CLINICAL STATUS
B. C.	F	1	1 week	Pneumonectomy, Rt., Oct. 1942	Epidermoid	Moderately decreased pulmonary function
H. C.	M	3	5 months	Pneumonectomy Rt., Dec. 1950	Epidermoid	Pulmonary status good
J. C.	M	4	2 months	Pneumonectomy, Lt., Dec. 1948	Epidermoid	Died 6 years postop. of unrelated disease
F. F.	M	11	2 months	Pneumonectomy Rt., Oct. 1951	Epidermoid	Well
C. G.	M	5	4 months	Pneumonectomy, Rt., Sept. 1952	Epidermoid	Well with slightly decreased pulmonary function
I. K.	F	No symptoms	31 months	Lobectomy Rt., Nov. 1950	Adenocarcinoma	Well; see Fig. 5
J. I.	M	2	1 month	Pneumonectomy Lt., Jan. 1943	Epidermoid	Moderately decreased pulmonary function
P. L.	M	2	None	Pneumonectomy Lt., Feb. 1950	Epidermoid	Psychotic; no evidence of recurrence
A. I.	M	16	None	Pneumonectomy Rt., Apr. 1951	Epidermoid	Died 5½ years postop. of unrelated disease
S. W.	M	5	None	Pneumonectomy, Lt., June 1952	Epidermoid	Died 5 years postop. with probable metastases

TABLE VIII. AVERAGE INTERVAL BETWEEN FIRST CLINICAL SYMPTOM AND CLINICAL DIAGNOSIS, PATHOLOGIC DIAGNOSIS, AND DEATH IN 359* CASES OF LUNG CANCER

	NO. OF PATIENTS	AVERAGE INTERVAL (MO.)	EXTREMES OF INTERVAL
Interval between first symptom and clinical diagnosis	359	6.8	0 to 60 mo.
Interval between first symptom and pathologic diagnosis	359	7.8	0 to 60 mo.
Interval between first symptom and death	305	13.8	2 wk. to 104 mo.

*One case had no recorded clinical history.

TABLE IX. AVERAGE INTERVAL BETWEEN THE EARLIEST RADIOGRAPHIC EVIDENCE OF LUNG CANCER AND THE CLINICAL DIAGNOSIS IN 350* CASES

	NO. OF PATIENTS	AVERAGE INTERVAL (MO.)
All cases	350	4.0
Excluding 153 cases in which earliest evidence coincides with the clinical diagnosis	197 (56%)	7.1
Excluding 238 cases in which the earliest evidence was less than 3 months from clinical diagnosis	112 (32%)	11.8
Excluding 276 cases in which the earliest evidence was less than 6 months from clinical diagnosis	74 (21%)	15.9

*Ten cases of series had no available x-ray studies for review.

TABLE X. AVERAGE INTERVAL BETWEEN THE EARLIEST RADIOGRAPHIC EVIDENCE OF LUNG CANCER AND THE PATHOLOGIC DIAGNOSIS IN 350* CASES

	NO. OF PATIENTS	AVERAGE INTERVAL (MO.)
All cases	350	5.1
Excluding 81 cases in which the earliest evidence coincides with pathologic diagnosis	269 (77%)	6.1
Excluding 215 cases in which the earliest evidence was less than 3 months from the pathologic diagnosis	135 (39%)	12.2
Excluding 238 cases in which the earliest evidence was less than 6 months from the pathologic diagnosis	92 (26%)	16.1

*Ten cases of the series had no available radiographs for review.

that, of the ten parenchymal lesions a centimeter or smaller in size, none was associated with any other radiographic change. However, half of those over a centimeter in size were associated with other abnormalities such as hilar enlargement, mediastinal nodes or pleural effusion, an indication of extension of disease. This is a strong argument for early excision of any questionable peripheral lesion.

3 *Hilar nodule* In 20 per cent of this series, a subtle increase in size of the hilar shadow was found, frequently best observed by comparison with a previous normal x-ray study In the majority of instances this change represented the direct evidence of the neoplasm (Figs 10 and 11)

4 *Hilar mass* Almost equal in frequency of presenting radiographic shadows was the much more obvious massive enlargement of the hilar shadow, a change making diagnosis much easier and prognosis correspondingly poor

TABLE XI TYPES OF EARLY RADIOGRAPHIC ABNORMALITIES FOUND IN 350* CASES PROVED TO BE LUNG CANCER

RADIOGRAPHIC FINDING	TOTAL		FOUND ALONE		WITH 1 OTHER ABNORMALITY		WITH 2 OTHER ABNORMALITIES	
	NO	%	NO	%	NO	%	NO	%
Obstructive pneumonitis	129	36.8	60	16.7	56	15.5	13	3.6
Parenchymal mass	77	21.4	45	12.5	24	6.7	8	2.2
Over 1 cm in size	67	18.6	35	9.7	24	6.7	8	2.2
1 cm or less in size	10	2.8	10	2.8	0		0	
Hilar nodularity	72	20.0	17	4.7	47	13.1	8	2.2
Hilar mass	69	19.4	35	9.7	25	6.9	9	2.5
Atelectasis	53	14.8	27	7.5	26	7.2	0	
Mediastinal nodes or mass	32	8.9	6	1.7	19	5.3	9	2.5
Pleural effusion	30	8.3	4	1.1	20	5.6	7	1.9
Parenchymal fibrous infiltrate	11	3.1	9	2.5	2	0.6	0	
Perihilar infiltrate	10	2.8	8	2.2	2	0.6	0	
Parenchymal mass with break down	8	2.2	6	1.7	2	0.6	0	
Obstructive emphysema	7	1.9	1	0.3	6	1.7	0	
Lung infection with abscess	5	1.4	3	0.8	2	0.6	0	
Diffuse parenchymal tumor	2	0.6	1	0.3	1	0.3	0	

*Ten cases of total series had no available radiographs for review

5 *Atelectasis* Atelectasis was found in 15 per cent of the patients Since all but one of these have died, complete obstruction of a bronchus from a tumor is considered by the authors as a poor prognostic sign Figs 12 and 13 illustrate a patient presenting with left lower lobe atelectasis which was thought to be an aortic aneurysm

6 *Parenchymal infiltrative density* An example of a carcinoma beginning as a vague fibrous infiltration is shown in Figs 14 and 15 This change is found with the same frequency as the small parenchymal nodule but is more often confused with old infection

7 *Miscellaneous*· Less frequent presenting radiographic changes such as fluid, emphysema, abscess, etc , are listed in Table XI

DISCUSSION

An average interval of almost 7 months between the first symptom and the clinical diagnosis emphasizes the continued need for improvement in cancer education of the public and the medical profession

Again, referring to Tables IX and X, an interval between abnormal shadows and diagnosis of 4 months for all cases, or

Fig. 1

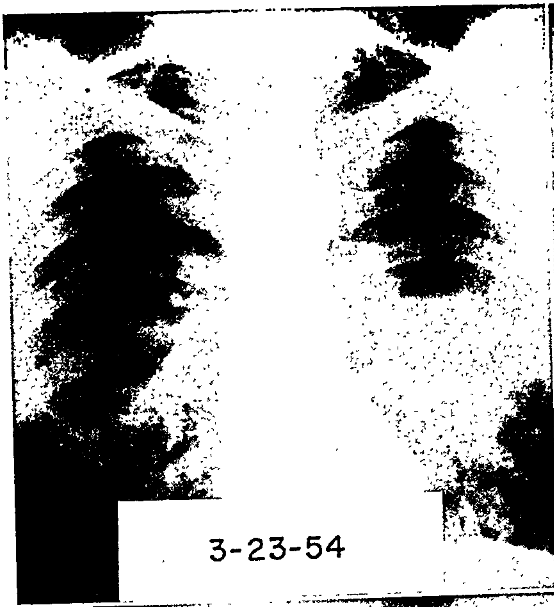
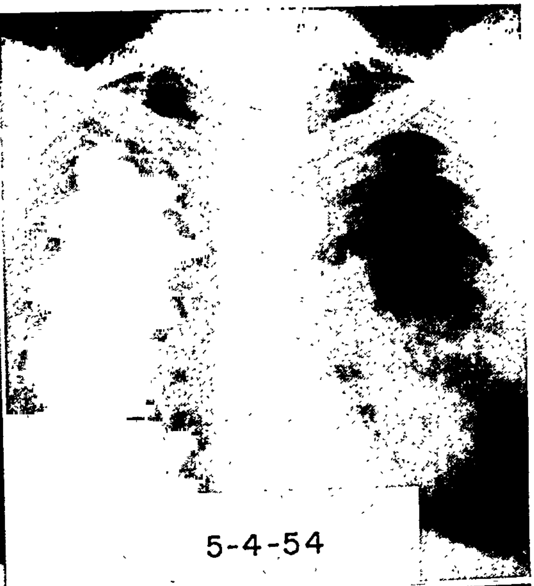


Fig. 2.



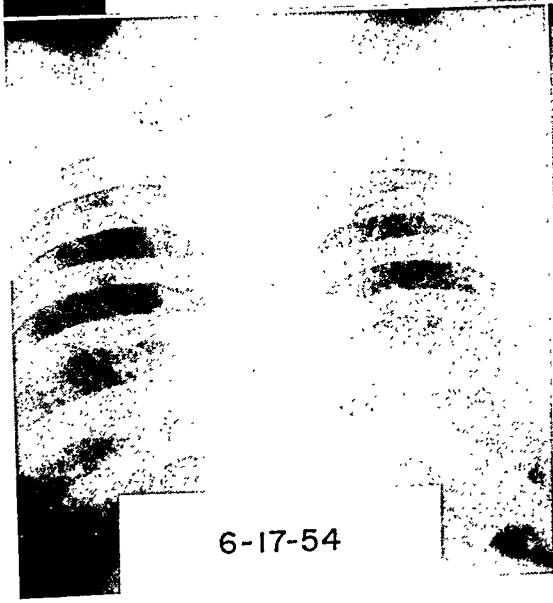


Fig. 3.

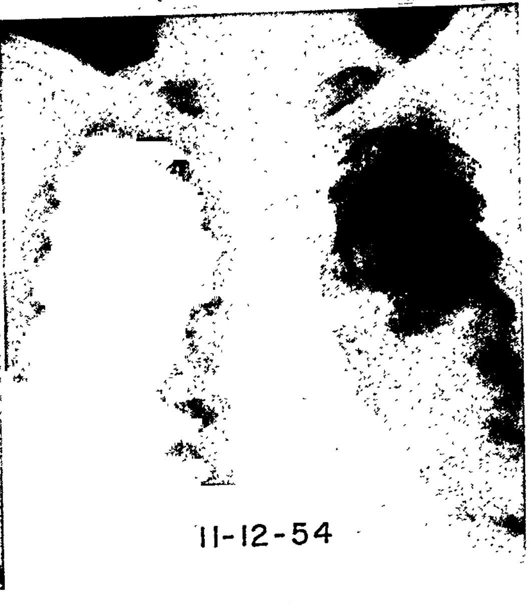


Fig. 4.

Figs. 1-4.—S. D., SMH No. 65317. A 47-year-old former truck driver with cough for the past 20 years which was worse following a bout of pneumonia 3½ years before. He had had frequent bouts of bronchitis. Patient was followed with x-ray studies which were interpreted as chronic pneumonitis for 7½ months during which time he lost 16 pounds in weight. Bronchoscopy and left pneumonectomy on 11/19/54 revealed epidermoid carcinoma. Patient is alive and well as of December, 1957. Progressive obstructive pneumonitis in the left lower lung field is seen in Figs. 1, 2, 3, and 4.

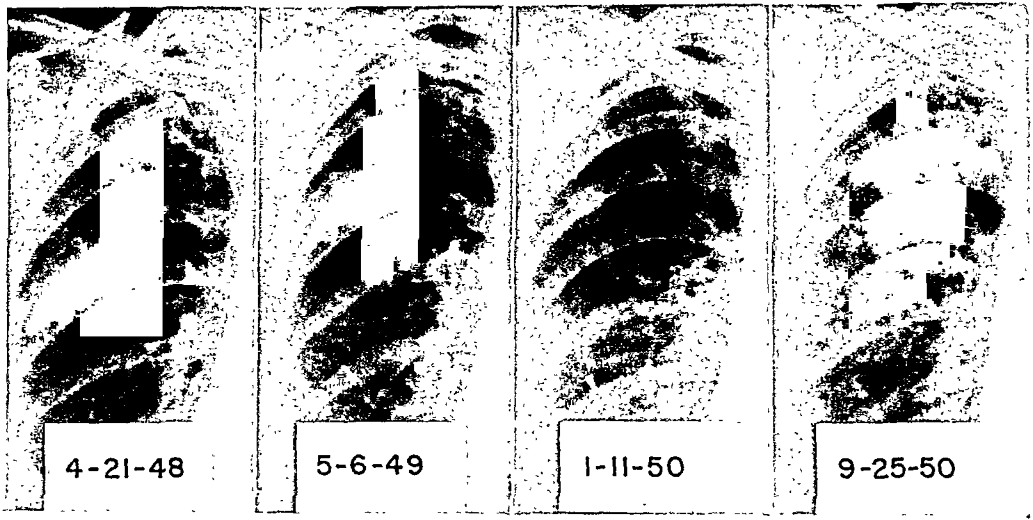


Fig. 5.—L. K., SMH No. 320241. A 53-year-old woman without symptoms. The lesion overlying the third rib anteriorly on film dated 4/21/48 was found on routine annual survey. Growth of the lesion on subsequent films over a period of 2½ years is evident, delay being primarily a medical responsibility. On 11/16/56 a right upper lobectomy revealed an adenocarcinoma. Patient is alive and well as of December, 1957.

Fig. 6

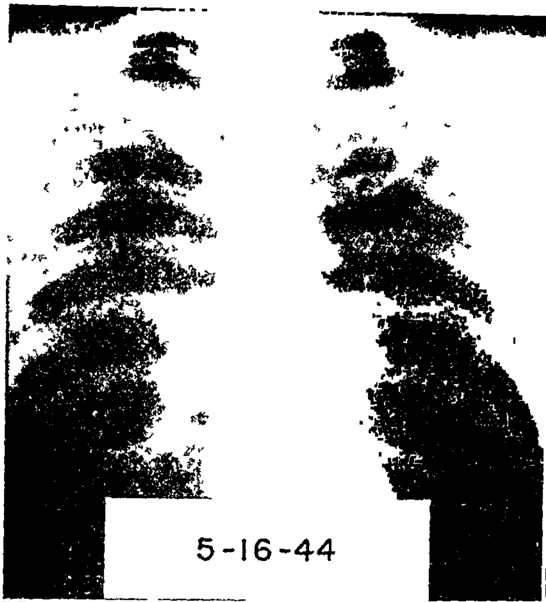
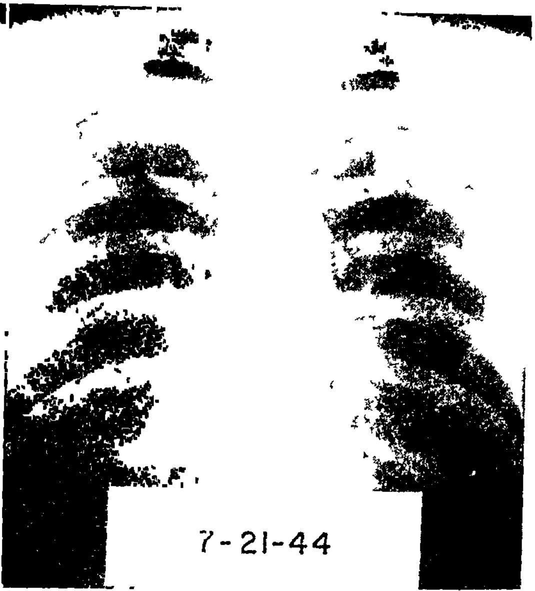


Fig 7



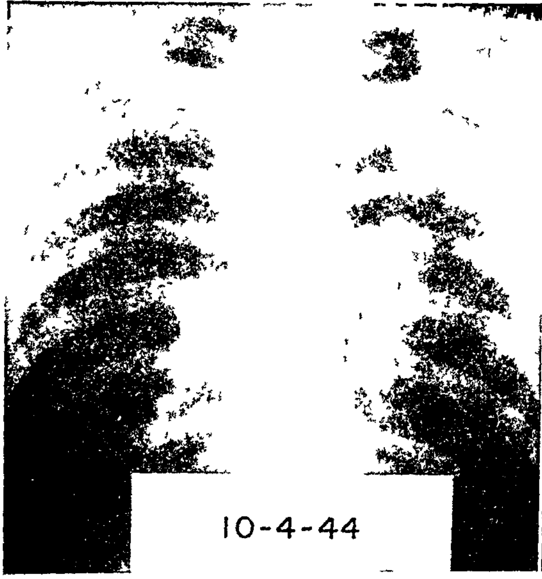


Fig 8

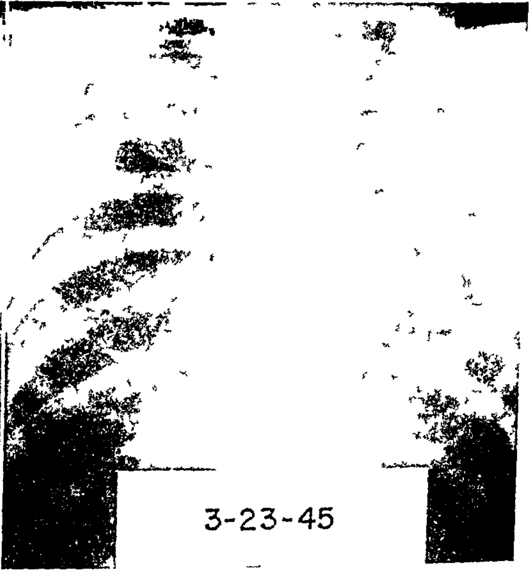


Fig 9

Figs 6-9 —A H, SMH No 230290. A 53-year-old male worker in a tuberculosis sanitarium with negative yearly chest roentgenograms from 1937 His first symptom of hoarseness did not occur until 3 months after the film illustrated in Fig 6 This was followed as tuberculosis without bacteriologic proof In contrast to the case in Fig 5, note the rapid growth of the lesion in the left upper lung field; also note rapid enlargement of the hilar shadow and mediastinal extension in 10 months (Figs. 7, 8, and 9).

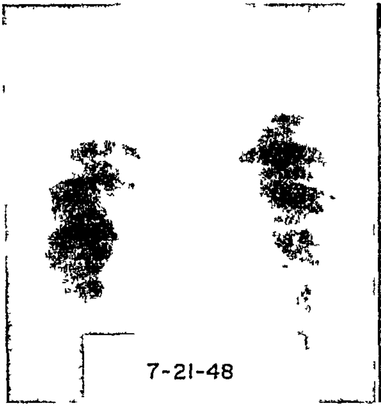


Fig 10

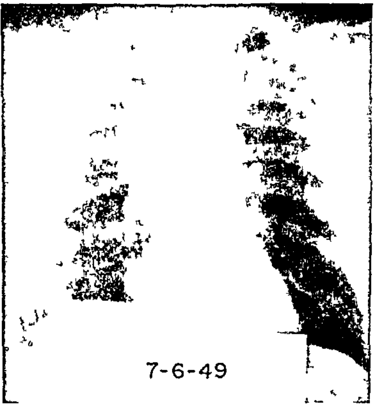


Fig 11

Figs 10 11—R W SMH No 298690 A 66 year old man admitted July 1949 with cough hemoptysis wheeze and a 20-pound weight loss during the preceding 2 months Chest x ray studies a year before admission (Fig 10) revealed an ill defined round density at the upper right hilum A year later this had enlarged with a considerable component of atelectasis of the right upper lobe as indicated by the elevated hilum and diaphram (Fig 11) Biopsy of a cervical lymph node revealed anaplastic carcinoma Patient died one month following a course of palliative radiation therapy

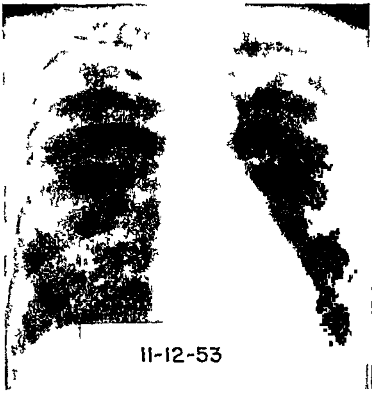


Fig 12

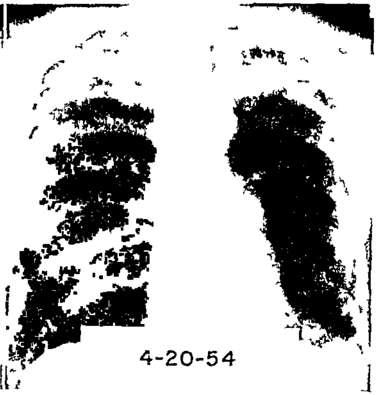


Fig 13

Figs 12 13—M Mc SMH No 181748 A 65 year old counterman admitted in November 1954 with increasing cough during the preceding 2 years and a 35 pound weight loss He had had negative chest films until 11/23/53 (Fig 12) when an interpretation of thoracic
le The dense shadow along the left heart border is actually an
with the outline of the heart border seen through it Five months
ollapse is shown with associated emphysema of the left upper lobe
revealed epidermoid carcinoma and thoratomy proved the lesion
died 9 months later

smaller, more significant group, plays a prominent part in the delayed diagnosis of pulmonary cancer. If we are to improve the cure rate, all methods to shorten this interval must be used.

The data relating to the early radiographic findings in cancer of the lung have emphasized that certain changes are highly significant. Hilar, mediastinal and large parenchymal masses, as well as gross atelectasis, produce radiographic shadows strongly suggestive of carcinoma and are of serious prognostic import. Somewhat less obviously produced by a cancer but to be viewed with a high degree of suspicion are obstructive pneumonitis, the small hilar nodule, localized emphysema, and thick-walled irregular abscesses. These carry a slightly less grave outlook, when diagnosed without delay.

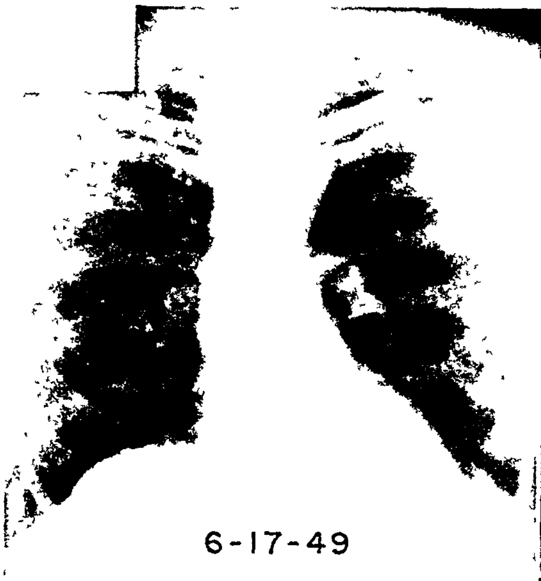


Fig. 14.

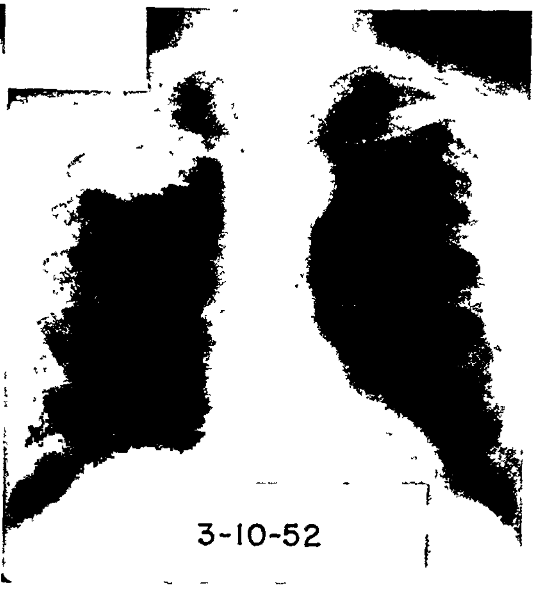


Fig. 15.

Figs. 14-15.—J. W., SMH No. 295160. A 58-year-old male reporter admitted in March, 1952, with fatigue, cough, and upper chest pressure. Admission chest film (Fig. 15) revealed a large right apical mass and review of a film taken 2½ years previously (Fig. 14) showed a faint fibrous infiltrate in the first right anterior interspace. At thoracotomy, the lesion was proved to be inoperable and biopsy revealed adenocarcinoma. Patient died 6 months later.

Much has been written recently about the isolated parenchymal nodule which the authors feel is malignant until proved otherwise.[6] As indicated above (Table XI), the smaller the nodule, the less apt it is to have other associated radiographic changes and the better is its prognosis. It is felt that the small persistent infiltrative density should be viewed with almost as much suspicion as the isolated nodule. It will most frequently be confused with a residual fibrous change from inflammatory disease and the distinction, on pure radiographic grounds, is often impossible with a single film. As in the study of changes in the hilar region, the review of current films with any other previous films is of great aid in evaluating the parenchymal nodule and infiltrative density. Even if there are no clues to the radiographic differentiation, the persistent parenchymal infiltrate warrants close follow-up and thorough clinical evaluation. The increase in number of resections now being done for these lesions should yield a better 5-year survival.

A definite factor in late diagnosis of carcinoma of the lung is the abnormal film which is read as normal. This will happen with even the most experienced eye and will not be completely eliminated. However, all efforts can be constructively directed toward keeping this factor to a minimum. In the case of mass survey examinations, it is frequently not trained radiologists or chest specialists who interpret the films but other physicians equally loath to miss a diagnosis but without the specialists' experience. In such cases, and even in the established x-ray department, the ideal would include double reading of films, particularly the normal films.

A very minimal change in the hilar shadow is frequently overlooked on a single film where it would be more obvious when compared with a previous normal film. Consequently, when a patient is being studied for possible chest disease, every effort should be made to gather all available past roentgenograms for combined study by the clinician and radiologist. In this regard, the destruction of chest films should be discouraged.

As indicated by Table IX, some 44 per cent of the patients in this series had no film taken prior to the time of diagnosis, or none was available. Yet, the changes present on admission films were such that many patients would have had positive radiographs if films had been taken during the preceding year. An increase in the frequency of films should, therefore, provide earlier case findings. In order to increase the number of chest films taken, the general increase in mass surveys in people over 40 years of age must be supported and patients must be encouraged to obtain periodic x-ray studies of the chest along with physical examinations. Where practical, the individual should be encouraged to have routine x-ray studies done at the same radiologic unit for better comparison follow-up.

Confronted with a suspicious shadow on a chest film and a consequent suspicious lesion in the thorax, it is mandatory that there be continuity of observation and patient care. Increasing numbers of patients suspected of a cancer of the lung today are given the advantage of modern methods of diagnosis. Where the working diagnosis of pulmonary cancer is made more promptly on first recognizing abnormal x-ray shadows, these diagnostic methods will be employed earlier in the course of the disease. It should be emphasized that a high index of suspicion will necessarily make more diagnoses than there are cases and one cannot presume that all suspicious lesions will turn out to be cancer. However, unless one presumes that they might, the toll of bronchogenic carcinoma will not be significantly reduced.

SUMMARY

This paper is a study of 360 cases of proved bronchogenic carcinoma with particular reference to the radiographic appearance of such lesions on any past radiographs before definitive diagnosis. Statistical information has been accumulated for general interest.

The average interval of time between early radiographic change and diagnosis for all patients was 4 months. In a selected group (considered more

significant) in which radiographs were available more than 6 months before diagnosis, this interval reached the alarming figure of almost 16 months.

The types of early radiographic changes are described. Methods of reducing the time interval between radiographic change and diagnosis and, thus, improving the current low cure rate, are discussed.

The authors wish to express their appreciation to Dr. Roger Terry, Department of Pathology, for his contribution in reviewing the pathologic sections, and to Mr. William Cornwell, of the Eastman Kodak Company, for his help in reproducing some of the radiographs.

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THE SCALENE LYMPH NODE BIOPSY

Gustav Bansmer, M.D., G. H. Lawrence, M.D.,** and*
*Lucius D. Hill, M.D.,** Seattle, Wash.*

Lymph nodes in the lower anterior cervical triangle and the retroclavicular area have long been recognized as a site of metastatic carcinoma from distant viscera. Virchow's node is a time-honored finding, classically indicating dissemination of a gastric carcinoma to the cervical lymph nodes. Lymphatic drainage of the body has been well plotted by anatomists, but the greatest familiarity was developed in those areas most commonly encountered by the surgeon. As a result, the lymphatic drainage of the thorax was of little clinical interest until the recent development of thoracic surgery. Although the lymphatic pathways of the thorax, pleura, and mediastinum have been documented by Rouviere,[3] much in advance of its practical usefulness, it was not until 1949, when Daniels[1] first demonstrated that the nodes overlying the scalene muscles could be sampled in order to gain histopathologic diagnosis of intrathoracic disease, that the work of the earlier anatomists became of pressing importance. In 1904, Delamere, Poirier, and Cuneo[2] showed that the lymph nodes of the lower cervical area also receive the drainage of the mediastinal lymphatics, and were not just a part of the drainage system of the head and upper extremities. Twenty-five years later, Rouviere[3] plotted the lymphatic fields of the lungs, pleura, and mediastinum and correlated the previous information.

Daniels' ability to make a tissue diagnosis of intrathoracic disease by biopsy of the supraclavicular nodes in 5 patients stimulated much interest in this area and more data became available for study. There is much confusion of terminology in the literature relative to this cluster of nodes and, at present, the term, scalene node, is becoming the most commonly used. Regardless of the term used, those nodes which lie in the fat pad over the anterior scalene muscle in the triangular space bounded by the carotid sheath medially, the omohyoid muscle supralaterally, and the subclavian vein inferiorly, are commonly called the scalene nodes. Even though they may be designated otherwise, the entity remains the same when the anatomic landmarks are the ones described. Rouviere's work has been of extreme value in developing the rule of thumb for selecting the site for biopsy.

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*Fellow in Surgery, Mason Clinic, Seattle, Wash.

**Department of Surgery, Mason Clinic, Seattle, Wash.

Harken[1] has stated this quite simply. If the lesion is right sided a right scalene biopsy only is done. If the lesion arises in the left lower half of the lung field, then a bilateral biopsy is done, and if the lesion is confined to the left upper lobe, only the left side is sampled. Figs. 1 and 2 show the outline of the lymphatic pathways of the lung fields. In addition to this rule of thumb, variations must be included. If there is only mediastinal disease, the side showing the most involvement is selected and if there is bilateral disease with neither side predominating, then both sides are biopsied. When there is sufficient suspicion that a lesion may have escaped the confines of the lung, a bilateral scalene node biopsy may yield a tissue diagnosis even if the most likely side is negative. There are intra-anastomotic channels which may permit cross metastases and, in selected cases in which the biopsy from one side is negative, it may be advantageous to include the opposite side even though it would not ordinarily fall into the route of drainage. When the scalene node biopsy is being done for extrapulmonary carcinoma, these rules do not apply. If abdominal carcinoma is suspected, the left scalene nodes are more likely to be involved because of their association with the thoracic duct. When there has been malignancy of extrapulmonary origin, the yield has been more rewarding on the left.[5]

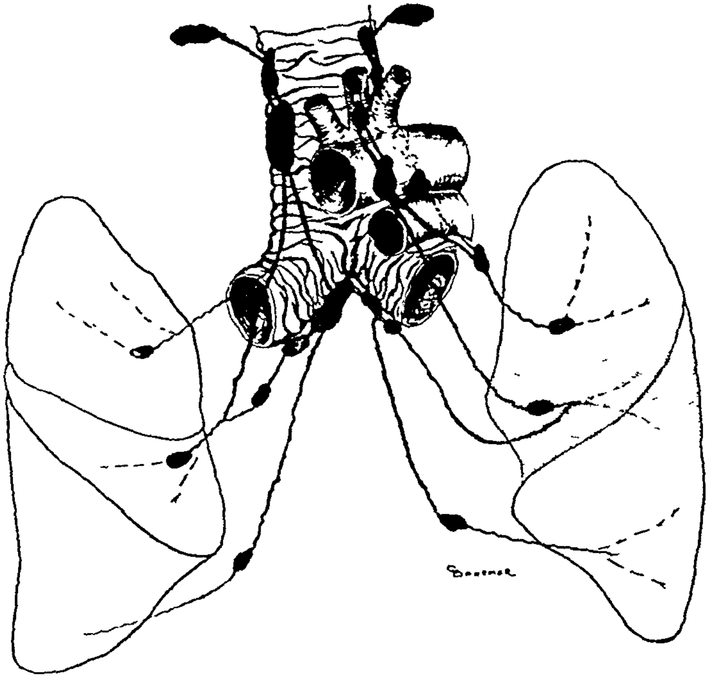

Fig. 1.—*Illustrates the drainage pathways from the lung fields with their termination in the scalene nodes (adapted from Rouviere).*

In the past 9 years since Daniels first published his results, there has been an increasing use of this diagnostic procedure. However, opinions vary as to its value and its indications. In the review of our own material at the Mason Clinic, it becomes evident that the frequency of scalene node biopsy has risen markedly. At the outset, biopsies were obtained sporadically but with greater use the impression arose that much useful information was obtained and a statistical review of our own data has confirmed these impressions (Table I) In order to evaluate further our data and compare it with the material available in the literature, a composite table has been drawn from previously published series and formed into a single group which includes the material available from this institution (Table II)

Our present policy is to perform (1) a scalene node biopsy on any patient with an undiagnosed pulmonary infiltrate and (2) prior to thoracotomy if a positive bronchoscopic biopsy has been obtained We feel a positive scalene lymph node represents a contraindication to further surgery Thus all prospective candidates for a thoracotomy in whom even the remote possibility of malignancy exists, are given the benefit of sampling of the scalene nodes before being committed to thoracotomy Boeck's sarcoidosis has such a high degree of pulmonary involvement that an increasing number of patients suspected of having Boeck's sarcoidosis are included in the group whose diagnosis and management may be most accurately planned on the basis of findings in their nodes

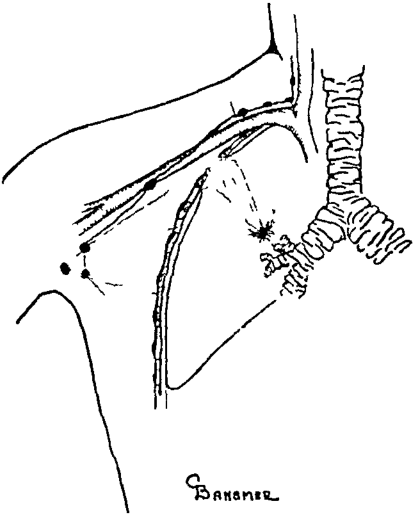

Fig 2—A schematic outline of the lymphatic drainage when pleural fusion has occurred (adapted from Ackerman and Regato)

Those patients who demonstrate metastatic bronchogenic carcinoma in the scalene nodes are not considered candidates for pulmonary resection even if the lesion were technically resectable This opinion is not unique to this institution and has been expressed by other authors[4, 8, 1] The opinion of nonresectability is based on the assumption that no benefit is [illegible] t[illegible] [illegible] by thoracotomy with or without pneumonectomy if t[illegible] shown evidence of escape not only beyond the confines of the lung, but also beyond those mediastinal lymph nodes which could be encompassed by mediastinal node dissection. The exceptions to these contraindications occur in patients who have persistent, severe bleeding, or where an abscess lies distal to the primary neoplasm. One other exception to this rule is found in those patients who on histopathologic study show minimal involvement by a carcinoma which is thought to be of low-grade activity; in these situations, thoracotomy may be attempted. It should be emphasized that this has not as yet occurred in our experience. In summary, we believe that a diagnosis of metastatic carcinoma of a scalene lymph node is valid evidence of nonresectability.

Although the primary use of the scalene node biopsy has been in either primary or metastatic pulmonary cancer, it is of even greater value in establishing a diagnosis of Boeck's sarcoidosis. Tumors of extrapulmonary origin have also been identified. Gastric, pancreatic, and breast carcinomas have been demonstrated in these nodes. Halsted originally included this area as a part of his dissection in radical mastectomy. In 119 patients, he found positive supraclavicular (scalene) nodes in 44, and of these only 2 survived 5 years postoperatively. Haagensen[6] has biopsied these nodes in an extensive group of cases, classifying as inoperable those cases with positive nodes. In addition to the metastases from remote carcinoma and involvement by sarcoidosis, the etiologic agent in the pulmonary granulomas, mycoses, and pneumonoconioses has been identified in the scalene nodes. It should be emphasized that nonpalpable nodes are in no way a contraindication to this diagnostic technique.

The technique is simple and is done under local anesthesia. A 3 cm. incision is made extending from the posterior border of the clavicular head of the sternocleidomastoid muscle posteriorly 1 cm. above and parallel to the clavicle. The platysma is divided. The sternocleidomastoid is retracted anteriorly and the omohyoid superiorly. The fat pad containing the nodes is exposed and is excised by sharp and blunt dissection. Palpable nodes if present, may be removed individually to shorten the procedure, following confirmation of diagnosis by frozen section. Likewise frozen section may be used if a two-stage procedure is contemplated. Recognition of the transverse cervical vessels and ligation, when possible, will reduce troublesome bleeding. The wound is closed and if the patient is being followed on an outpatient basis, a few hours of postoperative observation is all that is required. The complications have been minimal and consist mostly of serous or at times minimal chylous drainage. Pneumothorax has been reported. Simple measures will control the few complications that do arise.

Failure to obtain a diagnosis may have several origins, the most obvious being that there is no involvement of these nodes but, in general, one should expect involvement. The failure may be due to (1) inadequate removal of tissue from the proper area; (2) choice of incorrect side or failure to do both sides; and (3) blockage of more proximal lymphatic channels by tumor, preventing the extension of spread into the scalene nodes. We suspect the first reason as being the most common cause of failure.

RESULTS

One of the problems that initiated this review was to assess the over-all value of the scalene node biopsy in determining the operability of primary pulmonary cancer. Other observers have reported a yield of positive nodes varying from 6.3 per cent to 59.5 per cent. Shields and Shockett[22] believe the procedure has such a low yield that its routine use is not indicated when the lung is clinically resectable. In Table I the findings in 118 scalene node biopsies performed at The Mason Clinic are shown. Of the total number of patients with lung carcinoma in which a scalene node biopsy was done, 21 or 48.8 per cent yielded a positive diagnosis and were therefore spared a needless thoracotomy. In Boeck's sarcoidosis, a tissue diagnosis could be made in 14 out of 15 cases for a 93.3 per cent yield. In 13 additional cases of positive nodes, malignancy was of extrapulmonary origin. Of these, 2 were ovarian carcinoma, one gastric, a lymphoepithelioma, one a breast carcinoma, 6 lymphomata, and one in which the primary tissue of origin could not be identified.

One of the least common uses that has been made of this technique has been its value in identifying carcinoma of remote origin. We are at present directing its application to more of these cases. Schiff and Warren[5] studied the scalene nodes in 123 unselected cadavers which came to autopsy. A tissue diagnosis was possible in 16.3 per cent of all cases, but when this was further evaluated as to the number in which lymph node involvement could be expected to exist as part of the primary disease, the diagnostic accuracy rises to 43.5 per cent.

In summary, of the 118 biopsies a positive diagnosis could be made in 50 cases or 42.3 per cent. In the main, these lymph nodes were not palpable. Less than 6 per cent were described as palpable and in most instances there was lack of agreement as to whether the nodes were actually felt.

In the review of the published series available in the literature, a total of 1,916 biopsies was obtained. These data have been accumulated and summarized in Table II. In this composite series there were 616 pulmonary carcinomata wherein a scalene node biopsy was done. Of these 616 cases, 190 demonstrated metastatic carcinoma of the scalene lymph nodes or 30.8 per cent of all the primary pulmonary malignancies. Three hundred and thirty-four cases of Boeck's sarcoidosis were found and a confirmatory tissue diagnosis was made in 228 cases, or an over-all yield of 68.3 per cent. In regard to the diagnosis of Boeck's sarcoidosis where the series has been small, very high yields have been found, but it should be pointed out that as the size of the series enlarges the yield is less than when the selection is more intense. Table II also lists 112 cases of malignancy arising in the extrapulmonary tissues. Thirty-seven miscellaneous cases are listed and these are formed from tuberculosis, common nonspecific granulomata, histoplasmosis, and pneumonoconiosis. When the 1,916 cases are accumulated, an over-all yield of 34.1 per cent positive diagnoses are found.

TABLE I

AUTHORS	PULMONARY CANCER			BOECK'S SARCOIDOSIS			EXTRA-PULMONARY CANCER	MISCELLANEOUS	SCALENE NODE BIOPSIES		
	NO. CASES	NO. POSITIVE	PER CENT POSITIVE	NO. CASES	NO. POSITIVE	PER CENT POSITIVE			NO. BIOPSIES	TOTAL POSITIVE	PER CENT POSITIVE
Bansmer, Lawrence, and Hill	43	21	48.8	15	14	93.3	13	2	118	50	42.3

TABLE II*

AUTHOR	PULMONARY CANCER			BOECK'S SARCOIDOSIS			EXTRA PULMONARY CANCER	MISCELLANEOUS	SCALENE NODE BIOPSIES		
	NO CASES	NO POSITIVE	PER CENT POSITIVE	NO CASES	NO POSITIVE	PER CENT POSITIVE			NO BIOPSIES	TOTAL POSITIVE	PER CENT POSITIVE
Schweppert and MacManus[7]	71	6	8.5		4		6	1	122	17	12.3
Pulwan et al[8]	46	16	34				4		102	20	19.6
Cuykendall[9]	14	3	21	4	4	100	1	1	41	8	19
Umiker et al[1]	29	7	24						29	7	24
Hagensen							22		110	22	20
Connor[11]	29	9	31	5	4	80	1	3	38	17	45.5
Shefts et al[13]	24	13	54		38		7	9	187	67	35.5
Harken et al[4]	78	31	39.8	7			11	2	142	45	31.7
Carstensen et al[1]				237	148	62			304	168	55
Skinner et al[14]	53	24	45.3	5	5	100	11	2	100	42	42
Piper[15]		10		31	31	100	5	6	185	52	28.1
Yung[16]		9		1	1	100	11	4	42	25	59.5
Scott[1]	64	10	15.6	15	13	87	5	2	86	30	34.9
Kenney and Mota[18]		2		9			2	2	50	15	30
Felton and Spear[19]	22	6	27.2	1	1	100	3	1	35	11	31.4
Colombo and Musenti	65	12	18.5						100	12	12
Josephs and Woods[21]	78	32	41	3	3	100	10		125	46	37
Bansmer, Lawrence, and Hill	43	21	48.8	15	14	93.3	13	2	118	50	42.3
Totals	616	190	30.8	334	228	68.3	112	35	1,916	654	34.1

*These figures have been assembled and made into a composite series. Only those data have been used in tabulation in which sufficient information was available to lend statistical validity to the figures.

SUMMARY

The review of the material from The Mason Clinic was undertaken to catalog our own experience and lend support to the impression that the procedure is of value. In addition it was necessary to appraise the experience of others and evaluate our findings as compared with the total available composite series. An additional question arose as to the value of this procedure in identifying metastatic carcinoma arising in extrapulmonary tissues. In our own series, 43 cases of bronchogenic carcinoma studied by this method, a positive diagnosis was made in 48.8 per cent of the cases. Thirteen cases or 11 per cent of the total show metastases from distant viscera. The 15 cases of Boeck's sarcoidosis yielded positive data in 14 cases or 93.3 per cent. Two other cases show nonspecific granulomatous lesions. Thus, 42.3 per cent showed a positive diagnosis which was of value in the subsequent program of therapy in these patients. When a composite series was formed out of the groups available in the literature and the present series added to it, a more representative group is developed. In pulmonary carcinoma, 30.8 per cent of all cases yielded a positive diagnosis. In Boeck's sarcoidosis, 68.3 per cent of patients showed their disease in the scalene lymph nodes. Of the total group of 1,916 cases, 112 or 6 per cent had metastatic carcinoma arising in tissues other than the lung. Of this entire group in which scalene lymph node biopsies were done, 34.1 per cent of the 1,916 demonstrated their disease by involvement of these nodes and made a tissue diagnosis possible. By amalgamating the data from several sources the resultant figures are further supported by both larger samples and the loading of these figures can in part be offset by the diversity of the origin of the clinical material.

CONCLUSIONS

The scalene lymph node biopsy is of value in either primary or metastatic lung cancer.

A positive diagnosis of bronchogenic carcinoma in a scalene lymph node is a contraindication to further surgery except in a few specific instances.

Scalene lymph node biopsy should be a routine part of the study of any patient with a pulmonary infiltrate in whom a thoracotomy is planned.

Nonpalpability is not a contraindication to sampling the scalene fat pad.

Boeck's sarcoidosis shows a high percentage of involvement of the scalene lymph node.

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INTERMITTENT INFLOW OCCLUSION FOR THE DIRECT VISUAL REPAIR OF ATRIAL SEPTAL DEFECTS

Julian Johnson, M.D., Charles K. Kirby, M.D., William S. Blakemore, M.D., and Harry F. Zinsser, M.D., Philadelphia, Pa.

The early efforts to close atrial septal defects were not always successful but a few surgeons developed considerable skill in obliterating these defects without the aid of direct vision.[1-4] There can be no question, however, that there are many advantages to the methods which allow closure of atrial septal defects under direct vision. Complete closure is easier to obtain under direct vision, and other small defects, in addition to the major one, are much more likely to be recognized.

Many atrial septal defects have been closed successfully under direct vision, using either hypothermia[5, 6] or the heart-lung machine.[7-9] Using the heart-lung machine, the surgeon has more time and may use maximum care and deliberation in the definitive repair of the defect. The hypothermia technique is much simpler as far as cost and over-all effort are concerned. Even in those centers where the heart-lung machine is functioning satisfactorily, the difference in the amount of blood required to close an atrial defect under hypothermia and on the heart-lung machine is an item of considerable importance.

Our experience indicates that the two great hazards in the use of hypothermia in the closure of atrial septal defects are, first, the use of too severe degrees of hypothermia and, second, the use of too long a period of inflow occlusion. If moderate hypothermia (90° F.) is used and if the inflow occlusion does not exceed 4 minutes, there appears to be little if any risk in using this technique. While most atrial septal defects can be closed in that period of time, after the surgeon has had experience with it, there remains the occasional defect which requires more time.

There are three methods to increase the time available for closing an atrial septal defect under hypothermia. One is by using lower degrees of hypothermia, but this increases the risk of ventricular fibrillation with all the side effects and problems that accompany it. A second method is the utilization of an arterial transfusion into the coronary arteries through the base of

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From the Department of Surgery, Hospital of the University of Pennsylvania, the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania, and Edward B. Robinette Foundation of the Hospital of the University of Pennsylvania, Philadelphia, Pa.

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the aorta during the time of occlusion. While it is probably safe to use longer periods of inflow occlusion by this means, it is difficult to ascertain just how much time can be safely utilized. The third method of obtaining increased time for suturing when it is required, and the one which we prefer, is the use of intermittent inflow occlusion. Using this technique, the surgeon adds nothing to the risk of the vast majority of operations when the defect can be closed in the 4-minute interval, whereas he is in a position to obtain additional time in those instances in which it is required.

It has been our custom in the use of this latter technique to clamp the venae cavae first and start counting our time from that point. After about fifteen beats of the heart, the aorta is clamped and the clamp is removed from the incision previously made in the right atrial wall. In good-risk patients in whom the pulmonary artery pressure is relatively normal, very little blood has to be aspirated from the heart when the right atrium is opened. In the patient with pulmonary hypertension who is on the verge of heart failure, however, there may still be a fair amount of blood which has to be aspirated from the atrium in order to get adequate visualization. The important point is to get adequate visualization in the right atrium without allowing air to enter the left side of the heart. It has been our experience that if the septal defect is evaluated as completely as possible by finger palpation through the right atrial appendage before the atrium is opened, the surgeon is in a position to start sewing almost as soon as the atrium is opened. The clamping of the aorta is probably beneficial from two points of view. First, it stops the return of blood through the coronary sinus which allows a better visualization than might be obtained otherwise, thereby allowing a more rapid closure and, second, it probably cuts down the likelihood of air embolism.

If, after 3½ minutes, it becomes apparent that it is going to take more than an additional minute to complete the closure of the defect, we remove the clamps from the venae cavae, allow the atrium to fill with blood, close the atrium, and immediately remove the clamp from the aorta. The circulation is then restored for 10 minutes or so before using inflow occlusion for a second period of direct visualization to complete the closure of the defect. In this manner, it is theoretically possible to have an unlimited amount of time at the disposal of the surgeon. For practical purposes, most atrial defects can be closed with one 4-minute period and seldom, indeed, is it necessary to use more than two 4-minute periods of inflow occlusion. In our entire series, we have had only one patient in whom it was necessary to use three periods and a second patient in whom it was necessary to use four periods of inflow occlusion. In none of these patients has there been any complication from the repeated use of intermittent inflow occlusion.

In recent months, we have used the heart-lung machine (1) when we suspect a septum primum type defect, (2) when the heart is very large, suggesting that an Ivalon sponge might be required to close the defect, or (3) when there is severe pulmonary hypertension. We have hoped that the machine might give us some added safety in these patients. However, for ordinary atrial septal defects, we feel that the use of hypothermia offers a high degree of safety.

One problem which still remains in the use of either hypothermia or the heart-lung machine is that of air embolism. As far as we know, we have had only one air embolus in our series and that was due to a very obvious error in management. The anesthetist had not been properly briefed regarding the use of an adequate amount of muscle relaxant while the heart was open. The patient made a strenuous expiratory motion followed by a strenuous inspiratory motion which forced the blood out of the heart and sucked air into it. We immediately released the caval clamps to fill the heart with blood, closed the atrium and forced the residual air through the coronaries by manual compression of the heart. Fortunately, the patient recovered from this episode but it obviously could have been a serious accident. We had to use a second period of inflow occlusion to complete the closure of the defect but this was accomplished without difficulty. In recent months we have flooded the chest with CO_2 on the theory that if CO_2 is sucked into the circulation, it would be more rapidly absorbed than air.[10]

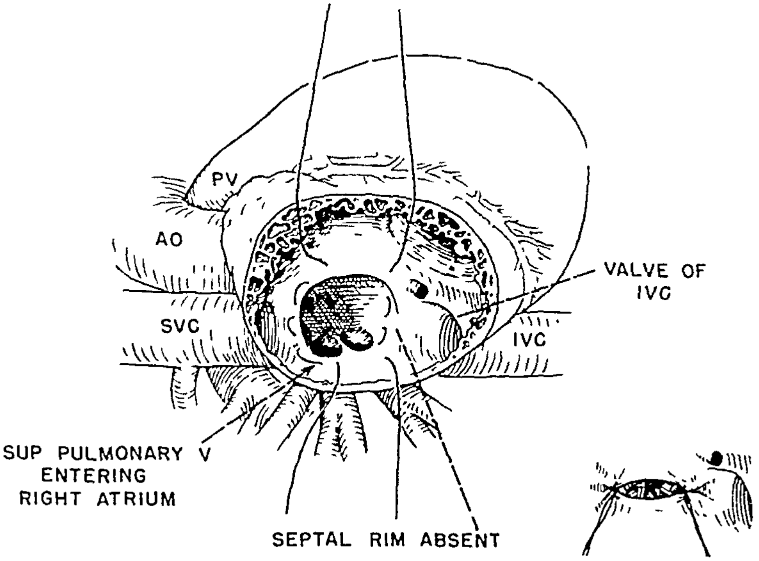

Fig. 1.—An atrial defect requiring a purse-string type suture both above and below is shown, although such a suture is seldom required at both ends of the defect. In placing the suture, less of the suture should remain within the atrium than shown, so as to allow complete approximation of the atrial wall.

Certain technical problems have been encountered in the closure of atrial septal defects. The secundum type of defect can be easily and rapidly closed by two continuous sutures which are started at either end and tied in the middle. When the right-sided pulmonary veins enter the right atrium, it is usually relatively simple to suture the anterior edge of the atrial defect to the right atrial wall in front of the opening of these veins. This allows the right-sided pulmonary veins to empty into the left atrium. In several of our patients, the opening of the defect did not correspond with the entrance of the right-sided pulmonary veins so that it was necessary to incise a portion of the septum, either upward or downward, in order to bring it to the right and in front of the pulmonary veins.

A deformity with no septal remnant at the posterior wall of the atrium, particularly at the lower border, has been encountered frequently. In these patients it is necessary to place a purse-string type suture, as illustrated in Fig. 1, as the initial suture in the closure of the defect.[6] Once this purse-string suture is placed, the remaining closure is very simple. In the patient who has an inferior vena caval valve, special care must be taken in placing the purse-string suture.[6] If the inferior vena caval valve were mistaken for the inferior border of the septum as the defect was closed, the inferior vena cava would then empty into the left atrium.

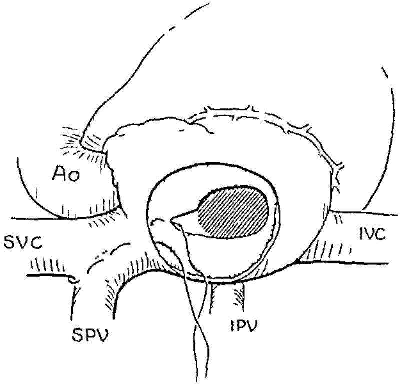

Fig 2 —In the defect shown the superior pulmonary vein joins the superior vena cava before it enters the atrium The septum was divided superiorly The purse-string type suture approximates the junction of the superior vena cava with the newly created cephalad end of the defect The anterior edge of the septum is then sutured to the atrial wall in front of the opening of the superior pulmonary vein, so that it empties into the left atrium. The superior vena cava continues to empty into the left atrium

A greater technical problem, but perhaps not so frequently encountered, is that of the right-sided pulmonary veins, or perhaps only the right superior pulmonary vein, entering the superior vena cava before it joins the right atrium. When this entrance is not more than an inch from the atrium in an adult, or perhaps less in a child, it is possible to use the same purse-string type suture in this area as that used below, partitioning the common vein following the junction of the pulmonary vein and the superior vena cava and causing the blood from the pulmonary veins to enter the left atrium and that from the superior vena cava to enter the right atrium (Fig. 2). In placing this purse-string suture either in this area or in the lower area, as described above, it is important that a minimum amount of suture remain within the atrium so that there will be satisfactory contact and a small opening will not be left between the stitches. When the right superior pulmonary vein enters the superior vena cava at some distance above the right atrium, the use of the purse-string suture, as illustrated in Fig. 2, does not seem practical. We have overcome this problem on one occasion by dividing the superior vena cava above the pulmonary vein and anastomosing it to the right auricular appendage after closing the atrial septal defect in such a manner as to use the proximal portion of the superior cava as a channel leading to the left atrium.

In our series of 65 patients with atrial septal defects, we have experienced some of the difficulties which may arise by the closed techniques. Also, we experienced some of the difficulties accompanying hypothermia of too severe a degree, as well as utilizing too long a period of inflow occlusion. Since the adoption of our present technique, however, namely, mild hypothermia and only 4 minutes of inflow occlusion at one time, we have felt that the closure of an atrial septal defect is about as safe a cardiac operative procedure as we have occasion to carry out. The risk of the procedure appears to be almost directly proportional to the severity of the patient's incapacity. One real problem exists in those patients with pulmonary hypertension with a right-to-left shunt. We are not entirely certain which, if any, of these patients should be declared inoperable and no attempt be made to close the defect. We now feel that in the patient without pulmonary hypertension this procedure can be carried out so simply, that we have advocated its use as a somewhat elective procedure during childhood if a considerable left-to-right shunt is present.

We have operated upon 45 patients with atrial septal defects, using the hypothermia technique. There have been no deaths in this series when our present plan of mild hypothermia and intermittent inflow occlusion was used. There were 4 deaths in the series, all in our early experience when in each instance the temperature was carried below 85° F. and in 3 the operative time exceeded 6 minutes for the one period of occlusion. It must also be admitted, however, that none of the 4 patients who died represented a simple septal defect. Two had pulmonary hypertension approximating the aortic pressure with right-to-left shunts and the other 2 had associated intracardiac lesions with one in severe heart failure. In each instance, it was recognized preoperatively that the patient presented a difficult problem, and the heart-lung machine would certainly have been used had it been available at that time. Whether it would have altered the outcome is problematical. One patient died following the closure of a defect after he went home. This was the man with a septum primum defect in whom we used 4 periods of inflow occlusion and who was discharged from the hospital in satisfactory condition. However, he suddenly went into heart failure and died about 2 months later. An autopsy showed that the suture had pulled away from the septum. Unquestionably at the present time, we would operate upon this man with the use of the heart-lung machine and put in an Ivalon patch. In our effort to not go too deeply in the region of the conduction system at the time of the closure of this defect, apparently we did not place the sutures quite deeply enough for them to hold.

Since our heart-lung machine has been functioning satisfactorily, we have used it for the repair of atrial septal defects in 7 patients because in each instance the problem seemed somewhat complicated. The only death in this group was due to a staphylococcic septicemia Our present policy is to use the heart lung machine in the repair of atrial septal defects when a septum primum defect is suspected, when there is excessive pulmonary hypertension or cardiomegaly, when the patient is in heart failure, or for any patient in whom it is thought that it offers an advantage over the hypothermia technique However, we believe that it is not necessary to use the heart lung machine for the repair of most atrial defects We believe that the hypothermia technique with intermittent inflow occlusion if needed offers minimum risk for the great majority of patients with atrial defects

SUMMARY

1 The use of mild hypothermia (90° F) and no more than about 4 minutes of inflow occlusion, with repeated periods of inflow occlusion if necessary has been safe and reliable for the closure of simple atrial septal defects under direct vision

2 Forty one patients with atrial septal defects have been operated upon by the proposed technique with no hospital deaths

3 The closure of atrial septal defects using the heart lung machine has been reserved for those patients who are poor risks because of advanced disease or in whom an unusual problem is suspected

4 Seven patients were operated upon with utilization of the heart lung machine because of some unusual problem The only death in this series was due to infection The chief objection to the use of this technique in all cases is the increased personnel required and the total effort expended, including the problem of blood procurement

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MITRAL INSUFFICIENCY WITH COMPRESSION OF THE LEFT MAIN BRONCHUS TREATED BY OPEN-HEART SURGERY

David R. Murphy, M.D., Anthony R. C. Dobell, M.D., Gordon M. Karn, M.D., and James E. Gibbons, M.D., Montreal, Canada

IN THE PAST year, surgeons[3, 4] have found it possible to achieve satisfactory short-term results in the treatment of mitral insufficiency by exposing the mitral valve during extracorporeal circulation and placing sutures across the posteromedial aspect of the annulus of the valve to reduce its diameter and permit coaptation of the aortic and mural leaflets. This operation, referred to as mitral annuloplasty, is similar in principle to the operation proposed by Nichols,[5] who used a blind technique. Reduction in annular diameter by a circumferential suture[2] has also met with some success in the treatment of mitral insufficiency.

Although left atrial pressure measurements have shown an encouraging drop, both in the experience of others[3, 4] and in several patients operated upon by us, it is evident that final evaluation of this operation must depend on long-term follow-up. The following case report was considered of interest because of the objective demonstration of sustained pressure reduction.

CASE REPORT

This young girl was first seen at The Montreal Children's Hospital in September, 1955. Past history did not reveal symptoms of acute rheumatic fever. A medical examination in March, 1955, had been normal. Physical examination disclosed a small child, weighing 33 pounds. The apical rate was regular at 80 per minute. The heart was enlarged with a forceful left ventricular apical impulse, 1 cm. lateral to the midclavicular line. A Grade 3 blowing pansystolic murmur was maximal at the apex and transmitted to the axilla; a mid-diastolic murmur was present. The diagnosis was rheumatic heart disease with mitral insufficiency. She was confined to bed for 9 months and in July, 1956, increasing activity was permitted. By the spring of 1957, she still was limited by fatigue and dyspnea and had not returned to school. During this convalescent period of a year and a half there was no indication of active rheumatic fever, but the heart size radiologically was definitely increasing (Fig. 1).

She was admitted to The Montreal Children's Hospital on Nov. 7, 1957, at which time she was 7 years old. She had had a persistent cough for several weeks and her exercise tolerance had decreased; dyspnea was present at rest as well as on exercise.

On physical examination she weighed 35.4 pounds, which was below the third percentile for her age. She was a poorly developed, pale, sallow child. There was no cyanosis

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From the Departments of Cardiovascular Surgery and Cardiology, The Montreal Children's Hospital, Montreal, Canada.

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and no clubbing of the fingers or toes There was respiratory distress at rest with a rate of 44 per minute The left chest moved only slightly with respiration The lower two thirds of the left chest was dull to percussion posteriorly and breath sounds were inaudible over the same area A persistent sinus tachycardia of 100 to 120 per minute was noted The blood pressure was 90/70 mm Hg There was a systolic thrill over the apex, which was situated in the sixth left interspace between anterior and midaxillary lines A Grade 4 blowing pansystolic and a Grade 3 rumbling diastolic murmur were heard at the apex There was an apical diastolic gallop The pulmonic second sound was accentuated The liver was palpable two fingerbreadths below the costal margin

Fig 1—Roentgenogram of the chest taken in June 1957 21 months after mitral insufficiency was first diagnosed

The electrocardiogram was interpreted as showing left ventricular and left atrial hypertrophy X ray studies of the chest (Fig 2) showed collapse of the left lung It was impossible to tell whether the heart had enlarged as compared to previous examinations because the left heart border was obscured by the atelectasis The opinion was that this patient had rheumatic heart disease with predominant mitral insufficiency, pulmonary hypertension, congestive heart failure, and atelectasis of the left lung

On November 19, bronchoscopy was carried out The left main bronchus was seen to be compressed by external pressure, leaving only a slit like orifice The compression was mainly anterior and was pulsatile Abundant secretions were aspirated from the left bronchial tree Vigorous medical therapy was carried out for 5 weeks, including digitalis, mercurial diuretics, antibiotics, and bronchial aspiration Nevertheless, deterioration was noted

Because of the grave outlook, mitral annuloplasty was performed on December 19, using extracorporeal circulation through the screen oxygenator* A right posterolateral thoracotomy was performed Care was taken to compress the right lung as little as possible

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*The Mark Company Randolph Mass

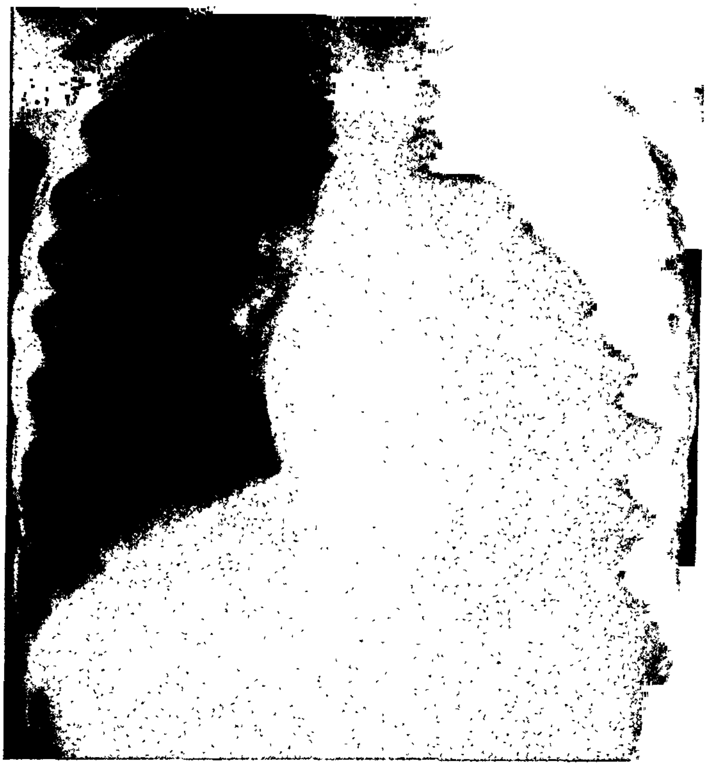

Fig. 2.—Roentgenogram of chest taken in November, 1957, demonstrating atelectasis of the left lung due to external compression.

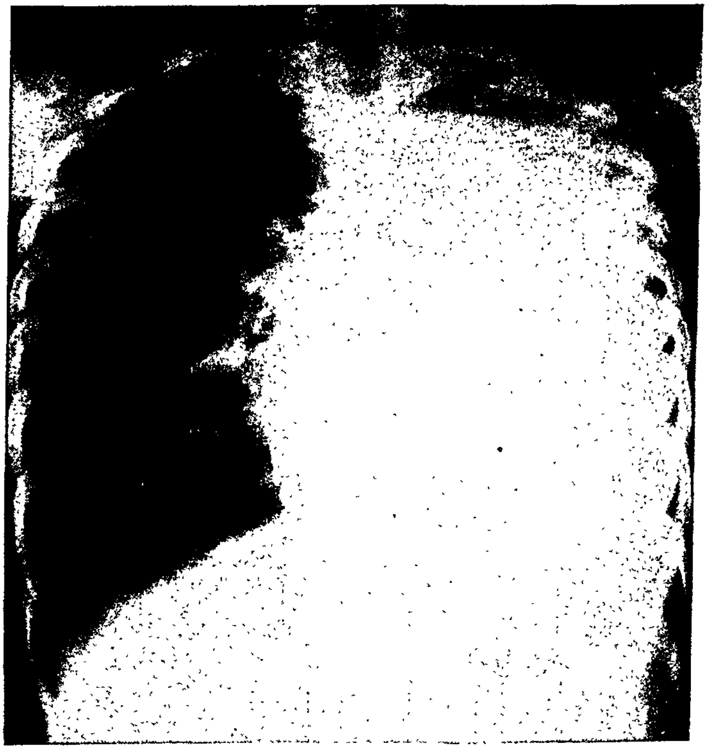

Fig. 3.—Roentgenogram of chest taken 3 weeks postoperatively showing re-expansion of the left lung.

The pericardium was opened anterior to the phrenic nerve exposing a large left atrium bulging posteriorly to the right of the right atrium. Because of the patient's condition, left atrial pressures were not taken before bypass. Catheters were inserted into the venae cavae, the inferior caval catheter having perforations in that part of it which was to lie in the right atrium so that the coronary sinus blood could be returned to the oxygenator. Arterial blood from the pump oxygenator was returned to the femoral artery. When cardiopulmonary bypass was instituted, the left atrium was incised and emptied of blood. The mitral valve was easily seen, both cusps were deformed by vegetations and the annulus was greatly dilated. A free regurgitant jet could easily be seen with each ventricular beat.

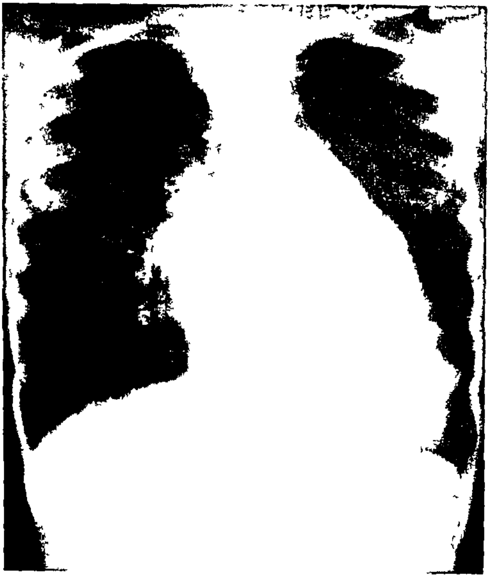

Fig. 4.—Roentgenogram of chest in May, 1958.

Five sutures of 2-0 silk were placed across the posteromedial aspect of the annulus so as to obliterate that commissure and permit the aortic leaflet to meet the mural leaflet. The regurgitation was all but eliminated. The atrial cavity was then filled with blood and the aortic leaflet was massaged against the anterior wall of the heart to ensure against the trapping of air in that location. The wall of the left atrium was closed and bypass was discontinued. Left atrial pressure measured after bypass was 12/5 mm. Hg, the systemic arterial pressure at the same time was 95 systolic. The atrium appeared much less tense than before annuloplasty. Following chest closure a tracheostomy was performed.

Her postoperative course was one of steady improvement. One week postoperatively the heart failure gallop and enlarged liver had disappeared. The tracheostomy tube was removed on December 28. Serial chest x-rays did not show aeration of the left lung until Jan. 11, 1958, when re-expansion was demonstrated (Fig. 3). She was discharged on Jan. 18, 1958, weighing 35.6 pounds.

By May, 1958, she weighed 44 pounds. The apical impulse was less hyperactive to palpation. There was a blowing Grade 3 systolic murmur. The apical diastolic rumble and the third sound had disappeared. There was no evidence of congestive failure. The lungs were clear (Fig. 4). Moderate activity, such as stair climbing, was performed without obvious fatigue or dyspnea. She was as active as she had ever been since the diagnosis of mitral insufficiency was made.

DISCUSSION

In the cases of massive dilatation of the left auricle reported by Daley and Franks[1] elevation of the left main bronchus was frequently seen either at its point of origin or within 3 cm. Schwedel[7] has stated that an enlarged left atrium frequently causes elevation and sometimes posterior displacement of the left main bronchus, but that actual compression is rare except in childhood.

Rivkin and associates[6] reviewed 8 cases of massive atelectasis of the left lung associated with increased pulmonary flow due to left-to-right shunts. All were infants varying from one to 16 months in age. In 3 cases, compression of the left main bronchus by the left pulmonary artery was demonstrated at autopsy and it was their opinion that this was the cause of compression in the remaining cases. One of their patients with total anomalous pulmonary venous drainage had an abnormally small left atrium, which certainly could not have compressed the bronchus. Total atelectasis of the right lung was not observed in their series.

In our case we are not certain whether the left bronchial compression was due to enlargement of the left atrium or pulmonary artery. We suppose that it was a combination of both factors, the left atrium compressing from below and the pulmonary artery from above.

SUMMARY

A case of mitral insufficiency with collapse of the left lung due to obstruction of the left main bronchus by vascular compression has been reported. The mitral valve was repaired by mitral annuloplasty using a pump-oxygenator. Three weeks later the bronchus re-opened and has remained patent since. Clinical improvement has been sustained for 5 months.

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CERTAIN BLOOD CHANGES IN PATIENTS UNDERGOING EXTRACORPOREAL CIRCULATION

Analysis of 350 Perfusions

Richard A DeWall, M D, David M Long, M D, Sharon J Gemmill, B S, and C Walton Lillehei, M D, Minneapolis, Minn*

CERTAIN alterations in the constituents of the blood are well recognized as a consequence of cardiopulmonary bypass procedures We have previously referred to some of these changes[1] [2] as measured in our patients perfused by the helix reservoir bubble oxygenator[3] [4] and the Sigmamotor pump during direct vision open heart surgical procedures The data herein recorded present, in more detail and in a larger series of patients, observations concerning the fate of red cells, platelets, and arterial pH, correlated with duration of the perfusions This information was derived from an analysis of the perfusion records of 350 clinical cardiopulmonary bypass procedures The types of cardiac lesions as well as the results of most of these operations have been described elsewhere[5] [6]

Duration of the Perfusions—Table I and Figs 1 and 2 indicate the durations of the perfusions analyzed in this series The patients have been divided into two broad groups on a basis of the substantial differences in their physiology The cyanotic† patients whose perfusion time had a mean duration of 46 minutes and the acyanotic‡ patients who were supported by the pump oxygenator for an average time of 27 5 minutes

Plasma Hemoglobin—Table I and Figs 1 and 2 indicate the plasma hemoglobin content of the patient's venous blood at the termination of these perfusions The method of Flink was used for these determinations The mean value for the plasma hemoglobin in the cyanotic patients was 70 mg per cent, having a rate of formation of 1 56 mg per cent per minute of perfusion The

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From the Department of Surgery University of Minnesota Medical School Minneapolis Minn

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*Advanced Research Fellow American Heart Association

†Tetralogy of Fallot complete transposition of the great vessels total anomalous venous return Ebstein's malformation

‡IVSD IASD pulmonic stenosis ruptured aneurysm of sinus of [illegible] mi [illegible] al aortic valvular heart disease ventricular and thoracic aortic aneurysm

mean plasma hemoglobin for the acyanotic patients was 46 mg. per cent which again was related to the duration of their perfusions, the rate of production being 1.64 mg. per cent per minute of perfusion.

Cardiotomy Loss.—Table I indicates the minute loss of blood from the perfusion system during these operations. As this blood was discarded from the perfusion system by means of a high vacuum suction system, it was measured and simultaneously replaced by reservoir blood. The cyanotic patients had an average loss of 40 c.c. blood per minute of perfusion while the average loss of the acyanotic patients was 43 c.c. blood per minute of perfusion.

TABLE I. SOME ASPECTS OF TOTAL BODY PERFUSION BY A PUMP-OXYGENATOR MEAN VALUES AND RANGE*

	DURATION OF PERFUSION IN MINUTES	PLASMA HEMOGLOBIN IN MG. %	PLASMA HgB. MG. % PER MIN. OF PERFUSION	CARDIOTOMY LOSS C.C./MIN. OF PERFUSION	ARTERIAL pH AT END OF PERFUSION
Cyanotic patients	12-105 — 46	5-155 — 70	— 1.56	— 40	7.15-7.60 — 7.41
Acyanotic patients	6-85 — 27.5	5-150 — 46	— 1.64	— 43	7.07-7.65 — 7.42

*The above information was abstracted from the perfusion and hospital records of 350 patients. In this series, approximately 25 per cent of the patients were in the cyanotic category. These data were not completely available on all the patients, however, 70 cases was the lowest number used to calculate any one of these values.

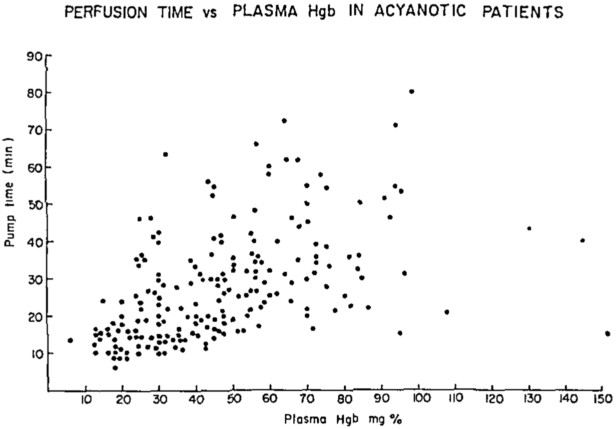
Postoperative Red Blood Cell Survival as Measured by Hemoglobin Determinations.—Hemoglobin determinations were charted daily in the postoperative interval for an unselected group of 35 patients. None of these patients received blood transfusions during the period in which they were followed. Decreases were observed in the hemoglobin values of these patients during this postoperative period. Table II indicates the mean values of these determinations.

TABLE II. POSTOPERATIVE HEMOGLOBIN VALUES* AFTER TOTAL BODY PERFUSION

PREOP.	DAY OF SURGERY	DAYS POSTOPERATIVE									
		1	2	3	5	7	10	12	15	20	25
14.5	14.6	14.8	13.9	13.1	12.1	11.8	11.5	11.8	11.6	11.8	11.9

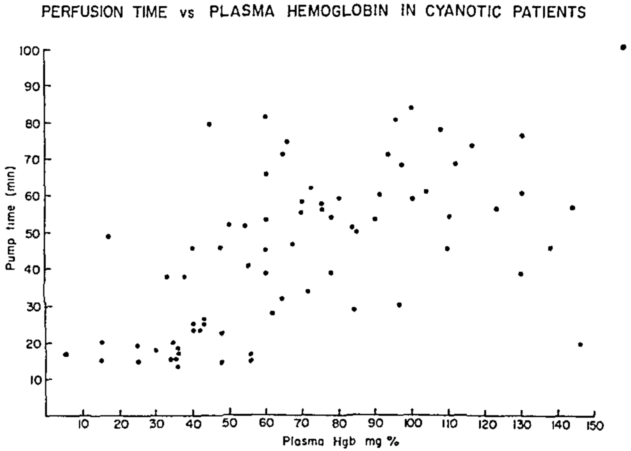
*In grams per cent. These are mean values from 35 unselected patients with a variety of intracardiac lesions who received no transfusions in the recovery period after the day of surgery.

Platelets.—In our previous reports,[1] we have analyzed the effect of total body perfusion upon platelet counts. Since we have never encountered postoperative hemorrhage due to abnormalities in the clotting mechanism, platelet counts are no longer a part of our routine patient care. However, serial platelet counts during the postoperative period have been determined in a series of 7 cases. In 4 of these patients an immediate drop in the platelet counts after the perfusion was observed (as in Fig. 3) while, in the others, the platelet counts were elevated above control levels in the immediate postoperative period followed by a fall during the next few days after surgery



PERFUSION TIME vs PLASMA Hgb IN ACYANOTIC PATIENTS

Fig 1—*The longer perfusions tend to be associated with the higher plasma hemoglobin* values which however at the highest levels are observed below concentrations that are likely to be of clinical significance



PERFUSION TIME vs PLASMA HEMOGLOBIN IN CYANOTIC PATIENTS

Fig 2—The rates of plasma hemoglobin formation during total body perfusion are about the same for cyanotic and acyanotic patients

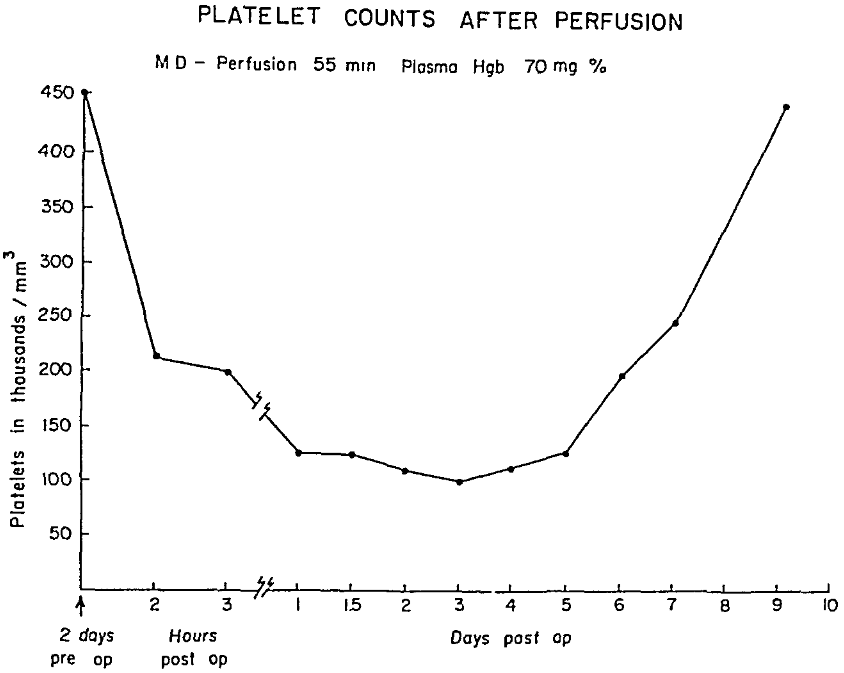


Fig. 3.—Platelet counts are observed to decrease from control levels after total body perfusion to return to control values within the first postoperative week. Regardless of the duration of perfusion, no patient has had a platelet depletion sufficient to cause hemorrhage.

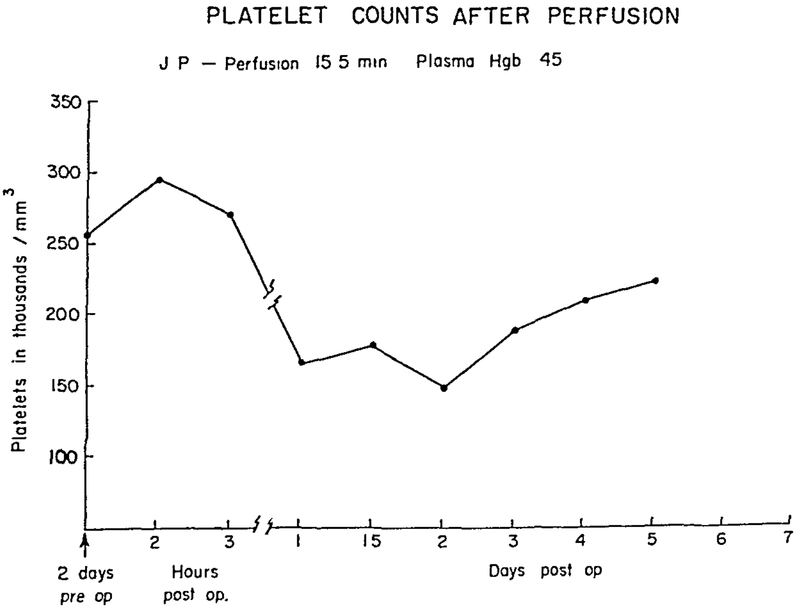


Fig. 4.—An elevation of platelet counts is observed in some patients as an immediate response to total body perfusion. The late response with these patients is a subsequent fall in platelet count then recovery within the following week.

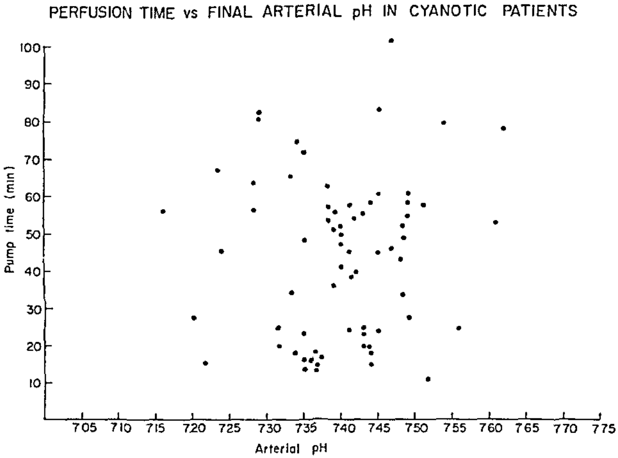


Fig 5—Perfusion time does not seem to have much correlation with the arterial pH of the patient at the termination of the perfusion Most values are observed within a relatively normal range regardless of the perfusion time

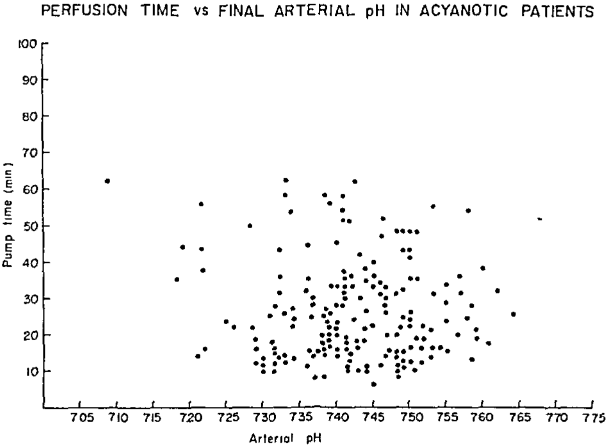


Fig 6—As seen in Fig 5 pH values do not seem to be a function of perfusion time

(Fig. 4). Beginning about 3 days after the perfusion, the platelet counts began to increase toward normal levels. Table III shows the mean values of these serial platelet counts as observed in these 7 patients.

TABLE III. MEAN PLATELET COUNTS* OF 7 PATIENTS AFTER TOTAL BODY PERFUSION

PREOP.	HOURS POSTOP.		DAYS POSTOP.				
	2	3	1	2	3	4	5
275	200	180	130	136	167	205	200

*In thousands per cubic millimeter.

Arterial pH as a Variable During the Perfusion.—The pH of these patients' arterial blood was determined just after the completion of the surgical repair. The blood samples were taken while the patient was still fully dependent upon the extracorporeal circulation, and before the lungs were inflated by the anesthesiologist. The scattergrams of Figs. 5 and 6 relate these pH determinations to the duration of the individual perfusions. Table I indicates the mean arterial pH values for the two groups taken at the time indicated above of 7.41 for the cyanotic patients and 7.42 for the acyanotic.

DISCUSSION

It is evident that changes induced in the blood as a result of total body perfusion are a function of time. The patients with cyanotic heart disease had lesions which required generally more perfusion time in order to be corrected (properly) than patients with acyanotic heart disease. Therefore, the perfusion times of these two groups were calculated separately. The duration of the perfusions for the acyanotic patients averaged about 40 per cent less time than that required for repair of the cyanotic patients (Table I). It may be noted that the plasma hemoglobin levels for the acyanotic patients were about 34 per cent lower than those observed for the cyanotic patients; however, as mentioned above, the cyanotic patients had longer perfusions during which plasma hemoglobin could be formed. The rate of plasma hemoglobin formation was actually a little less in the cyanotic patients than the acyanotic. The cyanotic patients have extensive bronchial collaterals, and they usually have a greater total cardiotomy loss* during the procedure than the acyanotic individuals. This does not seem to be reflected in the plasma hemoglobin values as Table I indicates. It was thought that perhaps the fresh blood added to the perfusion system to compensate for losses not retrieved by the cardiotomy suction system would decrease the measured plasma hemoglobin due to dilution. However, again on a basis of rate of loss (Table I), the perfusions on cyanotic patients actually lost less blood per minute from the system than that of acyanotic patients. Consequently, the plasma hemoglobin in the blood of cyanotic patients received no greater dilution than did the perfusion of acyanotic patients.

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*Cardiotomy loss is blood which spills through the incision in the heart and not successfully returned to the extracorporeal system. This source is mostly from the coronary sinus, thebesian veins, bronchial collateral, and occasionally from incompetency of the aortic valve.

About all that can be concluded from the above is that patients having cyanotic heart disease require longer surgical procedures and, therefore, longer perfusions than the acyanotic patients The rate of plasma hemoglobin formation in these two groups, as well as the rate of blood loss from the perfusion system is about the same As our experience has increased, less blood has been lost from the cardiotomy and the perfusion system than was the case with earlier bypass procedures In spite of this, the levels of plasma hemoglobin measured remain about constant This consistency seems to be true regardless of the arterial pump outputs required It is thought that most of the hemolysis observed is probably produced by the cardiotomy suction system which returns cardiotomy losses to the perfusion apparatus, however, the percentage that can be attributed to this is difficult to estimate The higher pump output rates used were not necessarily associated with higher plasma hemoglobin levels, but the longer perfusions were generally found to have higher plasma hemoglobin values in proportion to the duration of the perfusion The physiologic effects of the amount of hemolysis and any associated implications seen in these patients cannot be determined since, in all 350 patients, the final values of their plasma hemoglobin have been below that likely to be harmful In addition, we have seen no ill effects that could be attributed to these alterations in any patient

Our experience with platelet counts before and after perfusion have been previously reported,[1] however, the values were not observed on successive days for that study A decrease in the platelet counts is a consistent finding which is followed by a return to control values after a few days The decrease in platelet counts observed have all been to about the same level regardless of the perfusion time, or a short perfusion seems to show the same proportion of platelet lowering after surgery as does a long perfusion This has not been developed in a statistical manner Postoperative bleeding from deficiencies in the clotting mechanism has not been observed by us The occasional instance of postoperative bleeding that we have seen has been accounted for on a basis of inadequate hemostasis and since recognition of the importance of more meticulous hemostasis in these heparinized patients, unusual bleeding into the chest has not occurred Observations in our laboratory and conversations with others have led us to believe that bleeding problems in the postperfusion patient (or animal) can usually be traced to one of the following sources inadequately cleaned and sterilized perfusion equipment, blood incompatibilities or inadequate hemostasis The toxins of decomposing blood and bacteria (especially gram negative endotoxins) can produce lethal complications The helix reservoir oxygenator which we use comes in contact only with the blood of one patient and is then discarded Prior to use it is sterilized by autoclaving

A mild decrease in the patients' hemoglobin has been seen frequently in the postoperative period In part, this is a reflection of our efforts to keep the patients somewhat on the "dry side" during their first 24 hours after surgery by restricting fluid intake This produced some hemoconcentration during this early recovery period With the resumption of the oral intake of fluids, usually at the end of the first 24 hours, hemodilution [illegible] similar decrease in hemoglobin is, however, generally seen in any patient postoperatively, after major surgery and large blood exchanges. Many of our patients return to their homes within 14 days after surgery, consequently their hospital records did not have sufficient information concerning their postoperative hemoglobin values to be included in this study.

The hemoglobin studies in Table II were gathered from the records of patients who had longer hospital courses and who consequently reacted more severely to the procedure and exhibited the changes to a greater degree.

The metabolic changes produced by perfusion have been intensively studied in the past and previously discussed.[1, 2, 8] There is no longer a need to do them routinely, consequently the patient and the perfusion apparatus is now only subjected to "spot checks" for pH values. The acid-base balance of the blood is subject to many variables and an isolated pH value only tells of the general balance of these variables. For this purpose, a "spot check" pH is taken from *the patient's arterial blood at the end of the perfusion immediately* before the patient is artificially respired by the anesthesiologist. The scattergrams (Figs. 5 and 6) show that no obvious trend is present relating the arterial pH to the perfusion time. Among other factors, these values are dependent upon the perfusion rates.[6] The practice we currently use to establish a perfusion rate for a given patient has proved to be very satisfactory. The arterial pump* is precalibrated at various levels between 50 to 100 c.c. per kilogram of body weight per minute. When the bypass starts at the lower setting of the arterial pump, the systemic arterial pressures are monitored and the arterial output of the pump is increased as necessary to maintain normal electroencephalograms and mean systemic blood pressures. These patients do well with a perfusion of this type and no pH difficulties are encountered.

SUMMARY

The perfusion and hospital records of 350 total cardiopulmonary bypass procedures, utilizing the helix reservoir bubble oxygenator and the Sigmamotor pump, have been analyzed. These perfusions were done in conjunction with direct vision corrective intracardiac surgical procedures. The operative cardiac repair of cyanotic patients required about one third more perfusion time than did the repair of acyanotic patients. The rate of plasma hemoglobin formation was about the same in cyanotic and acyanotic patients. The platelet counts decreased after perfusion, but never to a degree to cause bleeding. A mild postoperative decrease in hemoglobin was observed during the first 3 weeks after surgery. Mean pH values at the end of the perfusion were within the normal range.

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THE DANGER OF HYPOGLYCEMIA DURING CARDIOPULMONARY BYPASS

Ervin L. Lobpreis, M.D., Los Angeles, Calif.*

THE ROAD to achieving a nearly ideal extracorporeal circulation is beset by many pitfalls, to the list of which must be added hypoglycemia. Unlike other problems connected directly with the construction and actual mechanics of the pump-oxygenator, such as adequate flow, oxygenation, acid-base balance, coagulation, embolism, and the like, this condition is related to the blood used for priming and replacement during the bypass procedure and to the changes of its chemical constituents in the course of time. The possibility of easily remedying this deficiency beforehand brings us one step closer to fulfilling one of the prerequisite features of the perfect artificial circulation, i.e., "that there must be little if any trauma, either chemical or physical, inflicted on the blood."[1] Hazards of the bypass procedure could thus be further reduced.

METHOD

Samples were taken from blood that had been collected in the currently available bottles (ABBO-Vac bottles containing 18 mg. of heparin in 30 c.c. of normal saline, intended for 470 c.c. of blood) and examined for blood sugar content at various intervals between withdrawal and actual use in the pump-oxygenator. Specimens of whole blood were processed immediately, employing the Somogyi-Nelson method for determining "true" glucose.[2]

Assuming that representative samples had been obtained each time after thorough mixing (inverting bottle 30 times), and postulating a straight-line relationship between blood glucose level and the time for each blood sample at any given temperature, the time of reaching the zinc-barium filtrate stage was taken, rather than the time of drawing the respective sample, in order to allow for the continuous sugar consumption.

RESULTS

The blood to be used for two bypass procedures, requiring 12 and 13 bottles, respectively, was sampled.

From the Department of Surgery, University of California Medical Center, Los Angeles, Calif.

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*Present address: Lt. E. L. Lobpreis, MC, U. S. Naval Hospital, San Diego 34, Calif.

The first series (Table I) included blood samples that had been drawn from the donors (most of them in fasting state) about 4 hours before being used for the patient. Determination I was done shortly after drawing the blood. Two blood bottles were kept at room temperature, the rest in a water bath at 37° C up to about 3 hours, at which time determination II was run. The calculated rate of 10.59 ± 0.31 mg per cent per hour corresponds to the rate of glucose consumption by the blood cells at body temperature. The blood was then mixed and used for priming the pump oxygenator. Twenty minutes before starting the bypass procedure, the glucose level of blood in the screen oxygenator was 44.2 mg per cent. The glucose level of the patient's arterial blood at this point was 125.2 mg per cent.

TABLE I. CHANGES OF BLOOD GLUCOSE LEVEL IN THE 4 HOUR OLD HEPARINIZED BLOOD

BLOOD NO.	I GLUCOSE (MG %)	TIME BETWEEN FILTRATES (MIN.)	II GLUCOSE (MG %)	DECREASE OF GLUCOSE (MG %)	RATE OF CHANGE (MG %/HR.)
1*	73.5	177	53.9	19.6	6.64
2*	71.6	176	47.4	24.2	8.25
3	62.6	182	28.1	34.5	11.37
4	73.5	180	36.1	37.4	12.47
5	73.5	180	45.8	27.7	9.23
6	75.2	179	45.8	29.4	9.85
7	136.5	187	103.9	32.6	10.46
8	73.5	161	49.0	24.5	9.13
9	67.7	165	39.4	28.3	10.29
10	71.6	162	45.8	25.8	9.56
11	103.9	164	69.7	34.2	12.51
12	80.6	161	52.3	28.3	10.55
13	78.7	161	49.0	29.7	11.07
	$m_{13} = 80.18$		$m_{3} = 51.00$		$m_{11} = 10.59$ $\Sigma d^2 = 10.8834$ $\sigma = \pm 1.04$ S.E. $= \pm 0.31$

*Room temperature.

The second series (Table II) consisted of blood samples drawn during the afternoon prior to operation (about 18 hours before use in the pump oxygenator) *from donors in various stages of the postprandial state.* The bottles were cooled both before and after drawing the blood and kept so for about 4 hours, when a sample for determination I was taken from each. Subsequently, the bottles were placed in the refrigerator and kept overnight. Determination II was made on the morning of the operation, just before placing the bottles in a warm water bath. The calculated rate of 1.39 ± 0.18 mg per cent per hour represents the rate of sugar utilization by the blood corpuscles at 4° C. Samples for determination III* were obtained 50 minutes before the bypass procedure and, since the blood sugar level dropped down to 25.59 mg

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*The blood samples of the second series were kept in a warm water bath between determinations II and III but, since the time period necessary for equilibration at 37° C from 4° C was not taken into account, the rate of change does not compare with the value obtained in the first series. It actually seems to approach the value for room temperature (see the first 2 bottles in the first series). The t test gives significant difference between these two values and since it is much less reasonable to presuppose that we are dealing with donors not belonging to the same general population, it depicts the influence of two temperatures that are not comparable.

TABLE II. CHANGES OF BLOOD GLUCOSE LEVEL IN THE 18-HOUR OLD HEPARINIZED BLOOD

BLOOD NO.	I GLUCOSE (MG. %)	TIME BETWEEN FILTRATES I – II (MIN.)	II GLUCOSE (MG. %)	DECREASE OF GLUCOSE (MG. %)	RATE OF CHANGE (MG. %/HR.)	TIME BETWEEN FILTRATES II – III (MIN.)	III GLUCOSE (MG. %)	DECREASE OF GLUCOSE (MG. %)	RATE OF CHANGE (MG. %/HR.)
1	81.5	746	67.9	13.6	1.09	225	50.3	17.6	4.69
2	85.1		70.6	14.5	1.17		37.9	32.7	8.72
3	60.7		54.8	5.9	0.47		11.2	43.6	11.63
4	70.8		48.2	22.6	1.82		16.8	31.4	8.37
5	67.9		49.7	18.2	1.46		13.7	36.0	9.60
6	76.2		51.2	25.0	2.01		25.5	25.7	6.85
7	70.8		64.3	6.5	0.52		25.5	38.8	10.35
8	70.8		51.2	19.6	1.58		22.4	28.8	7.68
9	70.8		60.7	10.1	0.81		25.5	35.2	9.39
10	70.8		51.2	19.6	1.58		28.6	22.6	6.03
11	67.9		36.3	31.6	2.54		2.5	33.8	9.01
12	81.5		60.7	20.8	1.67		47.2	13.5	3.60
	$m_{12} = 72.90$		$m_{12} = 55.56$		$m_{12} = 1.39$ $\Sigma d^2 = 4.12547$ $\sigma = \pm 0.61$ S.E. = ±0.18		$m_{12} = 25.59$		$m_{12} = 7.99$ $\Sigma d^2 = 60.4884$ $\sigma = \pm 2.34$ S.E. = ±0.68

per cent (average of 12 bottles), additional glucose—1 c.c. of the 50 per cent solution—was added to each bottle to raise the severely hypoglycemic level. It is easy to calculate that, had this not been done, a blood glucose level in the vicinity of 16.77 mg. per cent could have been reached by the beginning of the bypass procedure. The glucose level of the patient's arterial blood at this point was 133.5 mg. per cent.

Thus, the rate of glucose consumption by the formed elements of blood, calculated as 10.59 ± 0.31 mg. per cent per hour at 37° C., slowed down about 7.5 times during refrigeration at 4° C., yet did not cease entirely, since glycolysis was still going on at the rate of 1.39 ± 0.18 mg. per cent per hour.

DISCUSSION

Claude Bernard is said to have been the first one to observe, in 1876, that sugar disappears from blood in vitro. Gradually, it became obvious that the blood cells were not just inert cell remnants, but that they had a metabolism of their own which made a constant demand for a source of energy to sustain it. Macleod[3] demonstrated that the disappearance of sugar from blood in vitro was a function of its corpuscular activity. That these demands were appreciable was clear from his observation that about one half of the original amount of dextrose disappeared in 2½ hours from blood kept in vitro at 40° C.

Glucose, the substrate for this cellular glycolysis, is supplied by plasma. While in vivo the actual amount of sugar required by the blood cells may be insignificant in the over all carbohydrate metabolism, this need is quite definite and can be underestimated in vitro. On closer examination, it is evident that the heparinized blood collecting bottles in contrast to the A.C.D. bottles, are not enriched by an extra amount of dextrose. This is of still greater importance, because heparin—like hirudin and unlike oxalate[3]—does not retard glycolysis. From the above figures it is quite obvious that the rate of glycolysis in vitro, especially following incubation is fast enough to impoverish the plasma glucose and produce alarmingly hypoglycemic levels in the course of hours.

The vital importance of continuously maintaining the blood glucose level within a certain range has long been realized,[4, 5] and the body's ability to balance the dynamic equilibrium of glucose[6] has been recognized as an indispensable facet of the homeostatic mechanism. In this way, the "normal" blood glucose level is tenaciously maintained to meet all body needs. However, because of considerable individual variations both in health and disease it is not possible to draw a sharp dividing line below which a blood sugar level can be regarded as abnormal or at which the various symptoms and signs of hypoglycemia begin. The range of normal fasting values in whole venous blood, using the Somogyi Nelson method, is reported to be 65 to 110 mg. per cent, with an average value of 85 to 100 mg. per cent. Taking this as the normal range for "true" blood glucose, it has been generally accepted that levels below 50 mg. per cent mirror a serious situation, inasmuch as almost all subjects then display difficulties of one sort or another. Despite individual variations, levels below 20 mg. per cent are extreme and are usually encountered only during an insulin coma.

While there is no definite relationship between the duration of any particular hypoglycemic level and the severity of changes hereby produced, it is only logical to expect that the potential danger grows greater the longer a given hypoglycemic level lasts. In case of extracorporeal circulation, this would also depend on the volume of blood used during the bypass procedure and on the patient's own blood volume. When there is a considerable difference in the ratio of these volumes, increase of a blood sugar content to the normoglycemic levels (by the mixing of blood in the pump-oxygenator with the patient's own blood) is consequently delayed and a hypoglycemic state prolonged.

One more consideration, which is easily the most important single factor in a bypass procedure, involves the relatively great danger resulting from sudden change of a blood sugar level. It has been observed frequently in diabetics that a fast decrease of blood sugar content may produce symptoms, and even coma, although the actual blood glucose level is still above normal. Thus, the rate of fall is the determining factor irrespective of the absolute level reached and is most apt to bring on symptoms. And here we had a situation where the change was truly abysmal: with turning on the pump the patient's blood sugar level was abruptly reduced by about 80 mg. per cent in one case and, had this not been prevented, almost certainly by about 120 mg. per cent in the other.

Any combination of these factors (rate of fall, absolute hypoglycemic level reached, and its duration) does, of course, aggravate the situation. In case of the present pump-oxygenators, it is the considerable priming volume of blood (more or less hypoglycemic) which is of additive importance in relation to the initial headlong drop in the patient's blood glucose level. This is especially true in their use on infants whose blood volume (as little as 500 c.c. or even less) is suddenly confronted with an overwhelming charging volume of the pump-oxygenator (up to 5,000 c.c. or more). A temporary, acute hypoglycemia (relative or absolute) is the inevitable outcome. Its effects are almost instantaneous and the general nature of such a deprivation is comparable only to an episode of sudden massive bleeding or acute anoxia.

Outward results of this change are the chameleon-like manifestations of hypoglycemia, made more treacherous by concomitant anesthesia. Most of them are referable to the brain—cortex par excellence.[7] The cerebral metabolic activity is maintained by the blood-borne glucose on which the brain is almost exclusively dependent for its oxidative processes; and since oxygen and glucose are so singularly intertwined in the cerebral metabolism,[8] deficiency of the latter is tantamount to anoxia. So great is the brain's susceptibility to lack of either substance that—besides oxygen—a continuous, virtually second-to-second maintenance of the blood glucose level is indispensable for its functional and, eventually also, structural integrity. Prolonged hypoglycemia, on the other hand, results in an impaired cerebral function and finally in irreversible cortical changes accounting for the morbidity, for the various degrees of permanent functional decortication, and possibly even for the mortality itself.

As addition of an extra amount of dextrose to the heparinized blood collecting bottles offers itself as a logical measure to obviate this iatrogenic hypoglycemia, there are some details to be considered in this connection: how much sugar should be added, when, and what effect if any it might have on the blood, heparin and in turn, on the glucose itself.*

From the clinical standpoint, assurance of continuing normoglycemia or slight hyperglycemia (corresponding to the postabsorptive levels) is the objective. Since no long storage of the heparinized blood is being contemplated at the moment, raising existing glucose levels by an additional 100 mg. per cent would seem adequate for providing a sufficient margin of safety. Other things being equal, such a measure would allow about 70 more hours of refrigeration or 10 more hours of incubation. This is of particular advantage since it is frequently impractical to collect fresh blood immediately prior to its actual use.

Until the heparinized blood collecting bottles containing dextrose will be available commercially, additional 500 mg. of glucose (1 c.c. of the 50 per cent solution) per bottle can be introduced in the recirculating blood in the pump oxygenator or in the bottles themselves. Because of the danger of possibly contaminating the bottle contents during such an injection, this should be done just prior to the bypass procedure.

As for the possible interaction of the constituents in question—or rather the most probable absence of the same—so much can be said at the moment.

The possible hemolytic effect of glucose concentration below 2.3 per cent (osmotically equivalent to 0.45 per cent saline) and high dilution of serum[9] during the first impact of collected blood are offset by the presence of isotonic saline and by the fast flow of incoming blood. Since human erythrocytes are freely permeable to glucose at all its concentrations encountered in life, there is a rapid and uniform distribution of glucose throughout the total water of plasma and cells. By the same token, small increments of extra glucose, from any source[3] are also distributed evenly[10] and immediately[11] at body temperature. Moreover, the addition of extra glucose does not increase the rate of glycolysis.[3] At the same time there is hardly any doubt that glucose could be used up entirely in this process, because dilution of serum does not alter the permeability of the red cell membrane to glucose,[9] and metabolic demands of a viable cell are continuous. (Note in this respect the glucose level of 2.5 mg. per cent in the blood sample No. 11 of the second series.)

Heparin is a very stable polymerized polysaccharide containing both mucoitin sulfuric acid groups and glucosamine. Its anticoagulative properties are not destroyed by pancreatic extracts or prolonged boiling and apparently not even by bacterial action.[12] Some repository preparations of heparin now in use include dextrose as vehicle constituent, like *heparin in Pitkin's menstruum* with glucose in optimal concentration of 8 per cent. Heparin is being administered intravenously in normal saline or 5 per cent glucose and its stability in aqueous solutions is well known. While its stability in the saline-glucose solutions awaits further studies, it can be easily shown by protamine titration that the decline in anticoagulative action of heparin (both before and after addition of blood) in the saline-glucose solutions is not significantly different from that in normal saline, at least not in the first 24 hours and in the concentration of glucose as suggested.

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*By way of comparison it can be mentioned that the conventional A.C.D. blood bottles have 1.764 Gm. of glucose added (120 c.c. of the 1.47 per cent solution) to 480 c.c. of collected blood which gives an additional 294 mg. per cent in the transfused blood. Adding 0.5 Gm. (in 30 c.c. of the 1.6 per cent solution) to the 470 c.c. of blood in the heparinized bottles would give 100 mg. per cent in addition to the blood glucose level already present.

Provided bacterial contamination is prevented, no change of glucose can be anticipated in view of its similar saccharide nature and stability in acid medium such as is found in heparin solutions.

SUMMARY

There is a definite hazard in using the currently available heparinized bottles for collecting blood to be used during extracorporeal circulation. Since the bottles do not contain any glucose, only the native plasma glucose is used as the substrate for cellular glycolysis. The blood sugar level is thus gradually rendered hypoglycemic. This danger is considerably increased, if older (12- to 24-hour) blood is used when, following incubation, markedly hypoglycemic levels can be reached in the course of several hours. Apart from the absolute level attained and the variable duration of hypoglycemia, it is the precipitous drop of blood sugar level that is particularly objectionable with respect to its noxious effects on the cerebral function. Addition of extra glucose to the blood bottles as a simple and effective preventive measure is discussed and found sound and indicated.

CONCLUSION

Danger of a transitory, acute hypoglycemia during cardiopulmonary bypass is as real as it is preventable. To forestall its possible deleterious aftereffects, the contents of the heparinized blood collecting bottles should be enriched by a small amount of glucose. Addition of 500 mg. of dextrose to each bottle is recommended, preferably just prior to the bypass procedure.

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EXPERIMENTAL CEREBRAL EMBOLISM WITH ANTIFOAM A

J. Kiffin Penry, Captain, USAF (MC), A. Robert Cordell, M.D., Frank R. Johnston. M.D., and Martin G. Netsky, M.D., Winston-Salem, N. C.

INTRODUCTION

WITH THE ADVENT of open cardiac surgery, interest has been revived in the study of extracorporeal oxygenation of blood. Efficient oxygenators of various types have been developed. The older method of bubbling oxygen through blood is rapid and efficient for saturation of hemoglobin. Most of the currently used oxygenators, employing the bubbling principle, produce satisfactory hemoglobin saturation by dispersing oxygen in the form of tiny bubbles through the blood, thereby allowing the gas interchange at the bubble: blood interface. One of the greatest drawbacks to the use of the bubble oxygenator, however, has been the difficulty in defoaming blood adequately after oxygenation. The passing of blood over surfaces coated with a methyl polysiloxane resin (Antifoam A) is the most commonly used method of defoaming.

Clark and associates[1, 2, 3] were among the first to use this effective method of defoaming in a bubble oxygenator system. Following their example, many others have employed this resin as a defoaming agent in the many types of bubble oxygenators currently used. The general impression is that the resin is a nontoxic substance.[1, 5] We can find no report of any difficulty attributed with certainty to the use of this resin as a defoaming agent for bubble oxygenators. Rowe and associates[6] studied extensively the toxicity of certain commercial silicones and hydrolyzable silane intermediates. They found that methyl polysiloxane resin is low in chronic toxicity as judged by oral feeding to rats over a period of 400 days. Irritation of the skin was not produced by this material on prolonged contact, and only transitory irritation of the conjunctiva was found when the material was placed directly into the conjunctival sac. Intraperitoneal and subcutaneous modes of administration also were studied without evidence of systemic toxic effects. The intravascular route was not tested.

The resin is highly effective as a defoaming agent in concentrations of one to ten parts per million, if sufficiently dispersed.[6] The term *concentration* implies that a small amount of the material must be present in the diluting

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From the Department of Pathology, the Section of Neurology, and the Department of Surgery of the Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C.

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medium in order to have the material exert its defoaming effects. There is, therefore, no support for the concept that adherence alone to a debubbling surface is adequate for defoaming. A small amount of antifoam is necessarily present in the defoamed blood.

Because the vast majority of bubble oxygenators require blood to come in direct contact with this resin, the danger of embolic phenomena becomes apparent. Many investigators have suspected that antifoam causes some of the cerebral complications observed with the use of this material in bubble oxygenators. Giannelli and associates[7] studied the brains of dogs having undergone perfusion for 2 hours with a bubble oxygenator. They observed "lesions characteristically associated with embolism and infarction," but they did not demonstrate emboli in the brain. They observed tiny antifoam particles in the reservoir of oxygenated blood being perfused but did not see bubbles or fibrin. When an excess of antifoam was used, a greater number of lesions was found in the brains. They concluded that the cerebral lesions were embolic in origin but were unable to determine whether the infarcts were caused by air, fibrin, or antifoam emboli. Furthermore, adverse effects of antifoam have not yet been proved. DeCamp[8] and associates injected antifoam intravenously and into the aortic arch in dogs, but were unable to demonstrate abnormalities. The following experiments were undertaken to observe the cerebral effects of Antifoam A when injected into the internal carotid artery of the dog.

MATERIALS AND METHOD

Eight dogs were used, ranging in weight from 12 to 20 Kg. Injection of the internal carotid artery was performed in 6 dogs. Five of these received Antifoam A in heparinized blood; a sixth animal, serving as an experimental control, received only heparinized blood. Two additional dogs were sacrificed and used for control of the staining methods. The internal carotid artery of one was perfused with liquid Antifoam A to serve as a positive stain control; the brain of the other dog was not perfused and was used as a negative stain control.

All of the injections were into the right internal carotid artery. Each dog was anesthetized with intravenous sodium pentobarbital and an endotracheal tube was inserted. Aseptic technique was used. The carotid bulb was exposed and short lengths of the distal common carotid, the proximal internal carotid, and the proximal external carotid arteries were isolated. A loop of umbilical tape was placed around the distal common carotid artery and another around the proximal external carotid to immobilize the arteries when the injecting needle was introduced.

Venous blood was used for the injection of the experimental control animal and as the antifoam vehicle for the injection of 4 other animals. Blood from the femoral artery was used as the antifoam vehicle for the injection of 1 animal (Dog 5). The blood was drawn into a sterile syringe containing heparin and then discharged into a 50 ml. sterile beaker. Antifoam in either

TABLE I

DOG NO.	VOLUME OF ANTIFOAM A INJECTED (ML.)	TOTAL VOLUME OF BLOOD MIXTURE INJECTED (ML.)	PER CENT ANTIFOAM A IN BLOOD MIXTURE	DURATION OF INJECTION (SEC.)	IMMEDIATE RESPONSE TO INJECTION	DURATION OF LIFE AFTER INJECTION (HOURS)	CLINICAL SIGNS	MACROSCOPIC FINDINGS			MICROSCOPIC FINDINGS			SPECIAL STAINS	
								VASCULAR DILATATION	STAINING WITH TRYPAN BLUE	INFARCTS	MICROINFARCTS	FOCAL NEURONAL CELL LOSS	PERIVASCULAR INFILTRATIONS	OIL RED O	OSMIC ACID
1	1.0	7.5	13.8	15	Deeper, slower respiration	15	Remained comatose until death	+	+	−	+	+	−	+	−
2	0.75	11.25	6.7	50	Inspiratory howl, apnea, and death	0		+		−	−	−	−	−	−
3	0.1	6.6	1.5	180	None	48	Remained lethargic with loss of interest in food and surroundings	+	+	−	−	+	+	+	−
4	0.2	20.0	1.0	180	Deeper, slower respiration	48	Semicomatose for 24 hours after injection; subsequently, remained lethargic and was unable to stand	+	−	−	+	+	+	−	−
5	0.2	20.0	1.0	180	None	168	Semicomatose for 48 hours after injection; subsequently, remained extremely lethargic and was never able to stand	+	+	+	+	+	+	−	−
6	0.0	20.0	0.0	60	None	72	Normal	−	−	−	−	−	−	−	−
7	Negative stain control													−	−
8	Positive stain control (brain perfused with liquid Antifoam A after sacrifice).													−	−

liquid (Dog 1) or spray form (Dogs 2-5) was added to the blood and mixed thoroughly. The mixture was drawn into a sterile 20 ml. syringe through a 20 gauge needle, and all bubbles and air were eliminated carefully from the system. The total volume of antifoam injected was from 0.1 ml. to 1.0 ml., and the concentration of antifoam in the blood mixture ranged from approximately 1.0 per cent to 13.8 per cent (see Table I). The duration of injection was from 15 to 180 seconds. The left common carotid artery was occluded manually during two injections (Dogs 5 and 6) to increase the cerebral blood flow from the right internal carotid artery.

With the arteries immobilized by umbilical tapes, the needle was inserted into the lumen of the distal common carotid artery and advanced through the carotid bulb into the lumen of the proximal internal carotid artery. Traction on the arteries was released so that they lay in normal position. The injections of the mixture were continuous and timed (see Table I). When the injection was completed, the needle tip was withdrawn to the level of the carotid bulb and held for 3 minutes before removal from the vessel. Hemostasis was obtained by pressure, with care being taken not to interrupt blood flow within the carotid artery. The wound was closed in layers with interrupted black silk sutures. Trypan blue in isotonic saline (10 mg./Kg.) then was injected intravenously to detect an increase in capillary permeability.

The dog was returned to a warm recovery cage where hourly observations were made until recovery from anesthesia. Subsequent observations were made twice a day. At different intervals, up to 168 hours after injection, the surviving animals were anesthetized with intravenous sodium pentobarbital and sacrificed by transection of the thoracic aorta. The brain was removed immediately and suspended in 10 per cent formalin in isotonic saline solution.

After 48 hours in the fixative, the brains were photographed and sectioned in the coronal plane. Representative blocks were embedded in celloidin for sectioning at 20 microns and staining by the methods of Nissl and Weil. Other blocks were frozen and sectioned at 15 microns. Frozen sections were stained with oil red O,[9] and the facing sections with osmic acid.[10] Oil red O has been used for many years to stain fat[11], the staining is due to the solubility of this azo dye in the fat and not to a chemical reaction. The staining of antifoam by oil red O was demonstrated in vitro and in frozen sections of the brain (Dog 8) used as a positive stain control. In the osmic acid method, fat is rendered black by the deposition of osmium from a 2 per cent solution of osmium tetroxide, and thus this reaction is not based on solubility. Antifoam in vitro and in the positive stain control did not become black when the osmic acid method was applied. Therefore, when a substance is not rendered black by the osmic acid method, the material is not a fat.

RESULTS

The details of the individual experiments are shown in Table I. Abnormal clinical signs and histologic lesions were found in all animals receiving an injection of antifoam but were not seen in the experimental control animal

Slower, deeper respirations were observed in 2 animals during the period of injection. One of these animals remained comatose and died after 15 hours. A third animal responded to the injection with a loud inspiratory howl and apnea with immediate death. The injection did not evoke an immediate response in 2 other animals. The severity of the clinical signs differed widely in the surviving dogs. One animal (Dog 3) was lethargic with loss of interest in food and surroundings. Two others (Dogs 4 and 5) were semicomatose with severe generalized paralysis and required tube feeding. They improved within 1 to 2 days but remained lethargic.

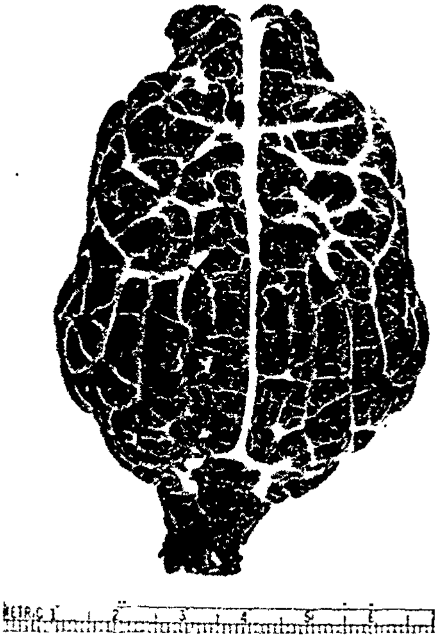

Fig. 1.

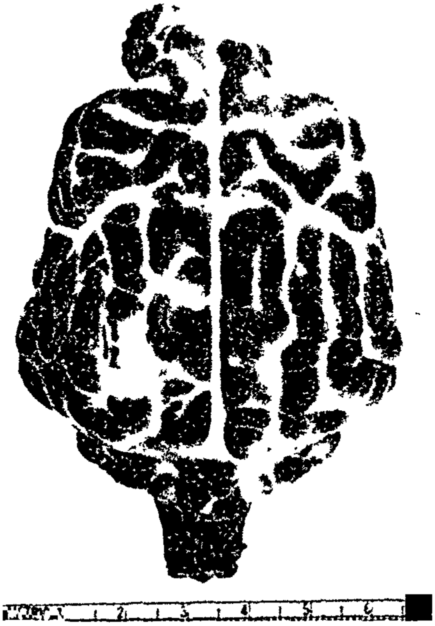

Fig. 2.

Fig. 1.—Photograph of dorsal surface of brain (Dog 1). The dilatation of the leptomeningeal blood vessels in the distribution of the right middle and both anterior cerebral arteries causes a dark appearance of these regions. The pallor in the region of the left middle cerebral artery is a striking contrast. Staining with trypan blue was seen, but it is not apparent in this photograph.

Fig. 2.—Photograph of dorsal surface of brain (Dog 5). There is a large hemorrhagic infarct on the surface of the left cerebral hemisphere. Numerous small infarcts are present in the lateral and ectolateral gyri of both cerebral hemispheres.

The macroscopic findings ranged from simple vascular dilatation to frank infarction. Fig. 1 illustrates dilatation of blood vessels in the region supplied by the right middle and both anterior cerebral arteries. Diffuse and focal staining with trypan blue was present in the region of dilated blood vessels. The most severe lesions were large and small hemorrhagic infarcts (Fig. 2). The findings on microscopic examination ranged from neuronal changes to infarcts with hemorrhage. The animal dying immediately was the only one without significant lesions of the parenchyma. Scattered foci of neuronal loss were seen in the cerebral cortex. These foci stood out in striking contrast to the normal tissue (Figs. 3 and 4). They were surrounded by neurons undergoing pyknosis, swelling and loss of Nissl substance. The small blood vessels in and around these zones were dilated and distended with

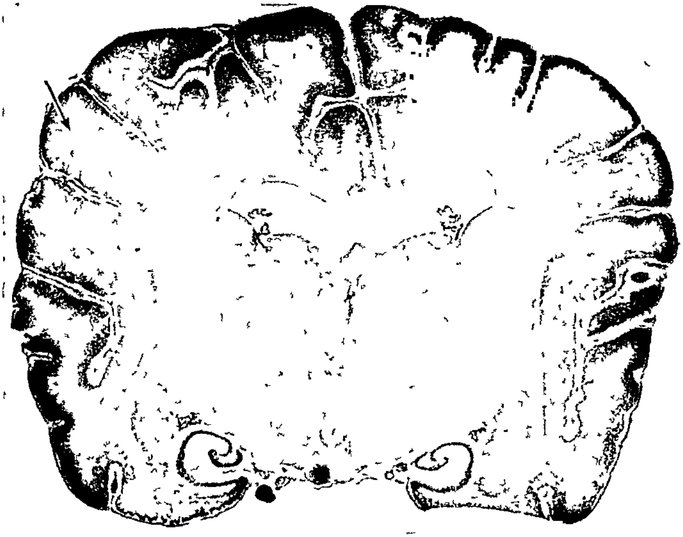

Fig 3—Macrophotograph of coronal section of brain (Dog 4) Small foci of loss of cells are scattered predominantly in the right cerebral cortex (on the viewer's left) (Nissl's technique × 3.6, reduced ⅕)

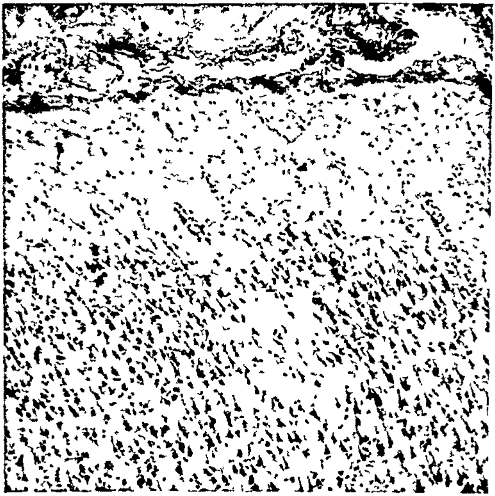

Fig 4—Photomicrograph of outer layers of the cerebral cortex (Dog 4) Neurons are decreased in number in the pale focus (Nissl's technique × 140, reduced ⅒)

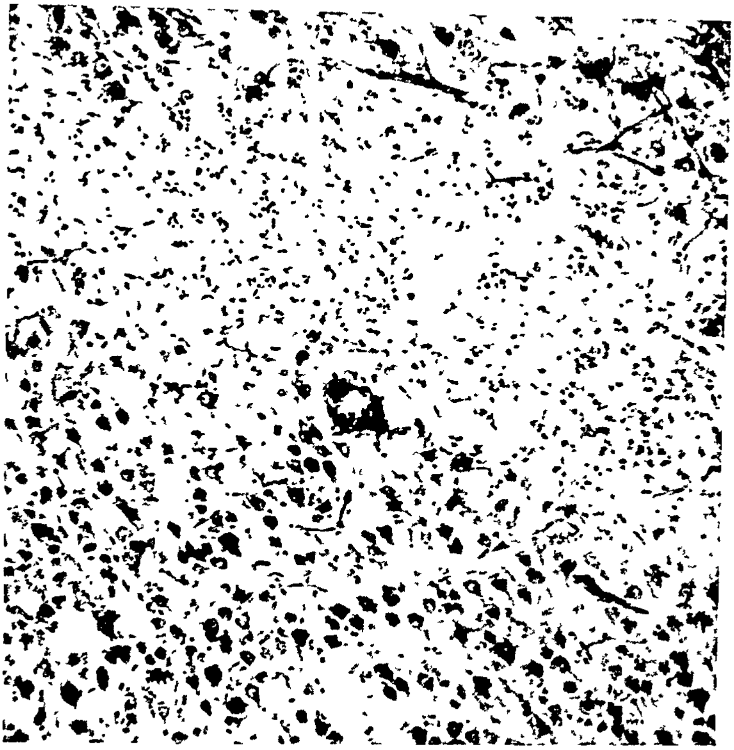

Fig. 5.—Photomicrograph of cerebral cortex (Dog 5) which shows a microinfarct. Note the loss of cells and complete destruction of the parenchyma, with infiltration of mononuclear cells. A single distended blood vessel is seen at the edge of the infarct. (Nissl's technique; × 140, reduced ⅒.)

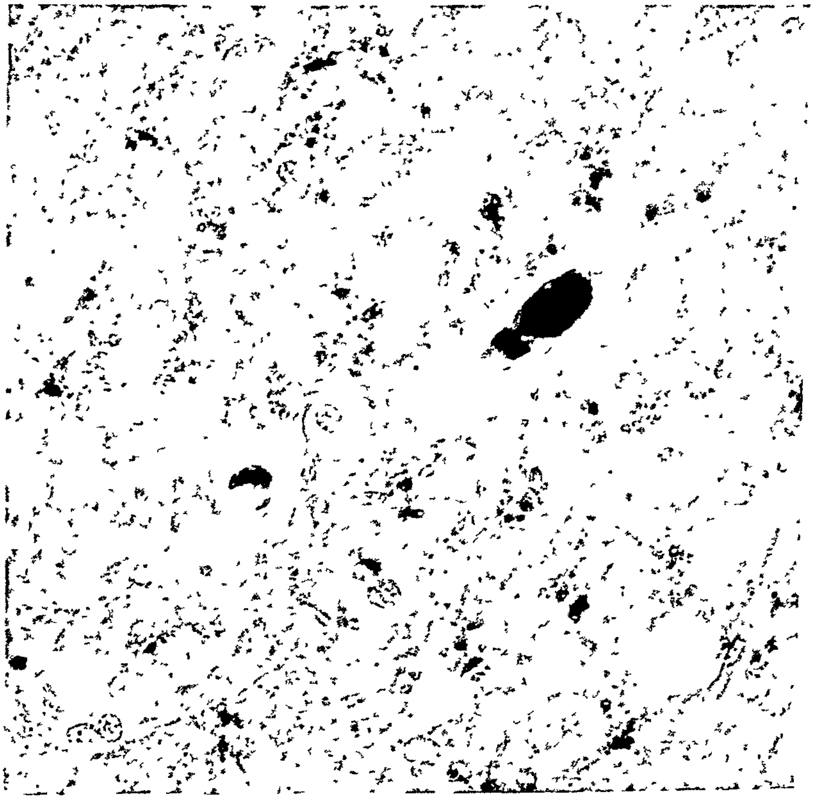

Fig. 6.—Photomicrograph of cerebral cortex (Dog 2). A blood vessel is distended and occluded by an embolus of Antifoam A. (Oil red O technique; × 480; reduced ⅒.)

blood. Small zones of demyelination were present less frequently in the subcortex. Perivascular infiltrates of mononuclear cells were sharply localized and were scattered mostly in the white matter.

The infarcts ranged from 0.1 mm. to 10 mm. in greatest dimension. The overwhelming majority of the infarcts were no greater than 1.0 mm. (Fig. 5). The largest infarcts contained small islands of preserved tissue, giving the appearance of numerous adjacent microinfarcts which had coalesced into a larger one. Hemorrhage into the infarcts occurred only in a few instances. Both gross and microscopic lesions were concentrated in the cortex of the parieto-occipital regions and were sparse in the frontotemporal regions. Lesions were rare in the basal ganglions.

Occlusion of capillaries and small arterioles by antifoam was demonstrated in all animals injected with this substance, but occlusion of larger blood vessels was not seen. In the frozen sections stained with oil red O, capillaries and small arterioles were filled and often distended with antifoam (Fig. 6). Material impregnated with osmium was not found within the blood vessels of the facing sections. Antifoam emboli were distributed widely throughout the cerebral cortex of the involved zones and were found infrequently in the subcortical white matter. The largest number of emboli was demonstrated in the animal dying suddenly (Dog 2). The 2 animals (Dogs 4 and 5) with the greatest quantity of parenchymal destruction had fewer occluded capillaries, but both survived a longer time.

DISCUSSION

Magendie,[10] in 1821, reported an experiment where he observed sudden death with occlusion of the small blood vessels after intravascular injection of oil. Antifoam is an oily substance with many physical properties similar to those of animal fats and oils, but it differs chemically. It should not be surprising, therefore, to find embolic occlusion of blood vessels after intravascular injection of this substance.

The primary lesion in antifoam embolism is the occlusion of capillaries and small arterioles. Immediate death, or coma and subsequent death of the animal result if many adjacent capillaries are occluded suddenly in a large part of the cerebral cortex. Large numbers of occlusions occurring more slowly result in coma and survival. The temporary loss of consciousness accompanies the interference with capillary circulation, but the persisting lethargy apparently results from the neuronal destruction. Microinfarcts are found in animals surviving more than 15 hours and are secondary lesions which develop after embolic occlusion of a small arteriole or of numerous adjacent capillaries. If the occlusions are sparsely distributed, only a few isolated neurons will die.

The data in Table I show that the clinical and pathologic findings are correlated with the number of emboli and rate of capillary occlusions. Two animals (Dogs 1 and 2) received a large number of emboli rapidly. One of these died immediately, and the other survived in coma for only 15 hours.

Two other animals (Dogs 4 and 5) received a small quantity of emboli slowly and survived. After recovery from coma, lethargy and paralysis persisted. Only lethargy resulted when a very small quantity of emboli was given to another animal (Dog 3). The emboli were few and widely distributed; they did not cause extensive interference with capillary blood flow.

The *animal dying suddenly had the greatest number of capillary occlusions* because a large number of antifoam emboli was injected, but insufficient time elapsed for removal of the embolic material. Infarcts were not found because the animal died too quickly. The brain appeared normal on macroscopic examination except for vascular dilatation. The only lesions on microscopic examination were numerous antifoam emboli. In the other animals receiving antifoam, staining of the brain by trypan blue gave evidence of increased capillary permeability. The pale infarcts caused by antifoam often were seen only on microscopic examination.

Our experimental findings are comparable in many respects to those found in cerebral fat embolism.[13, 14] In the latter, widespread occlusion of small vessels is accompanied by lethargy and coma. If death does not occur, recovery begins after a few days. Localizing neurologic signs are rare and usually are associated with other complications. The fat emboli either pass through the capillaries or are removed by macrophages. The small foci of destroyed tissue undergo glial repair, but the damage may not be apparent in the behavior of the patient. In those dying in coma, the pathologic findings are occlusions of small blood vessels by fat, perivascular hemorrhages, demyelination, and microinfarcts. The latter two lesions are not found if death occurs immediately after the onset of coma. The only striking difference between fat and antifoam embolism is the paucity of perivascular hemorrhages in our experiments. The hemorrhages so prominent in cerebral fat embolism may be associated with hypoxia and other disturbances secondary to capillary occlusions in other organs. Our pathologic findings also are comparable to those of Swank and Hain[15] in their study of microembolization with paraffin.

The cerebral distribution of the emboli is interesting because the microinfarcts are concentrated in the parieto-occipital regions, are sparse in the frontotemporal regions, and rare in the basal ganglions. The regions receiving the largest number of emboli, therefore, are those supplied by the terminal leptomeningeal divisions of the middle and anterior cerebral arteries. The terminal divisions divide from the main trunk at small angles, but the proximal divisions supplying the basal ganglions branch at right angles. It appears that the angle of branching and the size of the main division influence the distribution of these emboli.

CONCLUSION

Antifoam when injected in sufficient amount into the cerebral arterial system can cause sudden death, or coma and subsequent death. Cerebral infarction results if enough time elapses after injection. Capillary occlusion by antifoam can be demonstrated by the oil red O technique in frozen sections and differentiated from fat by the osmic acid method The clinical and pathologic findings in cerebral embolism with antifoam are comparable in many respects to those observed in cerebral fat embolism

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THE ELECTROENCEPHALOGRAPHIC EFFECT OF COMPRESSION OF THE SUPERIOR VENA CAVA DURING THORACOTOMY

Verne L. Brechner, M.D., Eva M. Kavan, M.D., and John B. Dillon, M.D., Los Angeles, Calif.

IT HAS LONG been appreciated that electrical cortical activity accurately reflects depth of anesthesia. Gibbs, Gibbs, and Lennox[1] recorded electroencephalographic patterns during ether anesthesia in 1937. At that time, they were able to correlate depth of anesthesia with the various recorded patterns, and suggested that the electroencephalogram be used to monitor depth of ether anesthesia. Rubin and Freeman[2] reported some of the electroencephalographic changes associated with cyclopropane in 1940, and Brazier and Finesinger[3] conducted a similar investigation with barbiturates in 1945. In 1950-1953, Faulconer,[4] Courtin,[5] Possati,[6] Kiersey[7] and their associates classified the electroencephalographic patterns seen during diethyl ether, nitrous oxide, cyclopropane, and Pentothal anesthesia, correlating the patterns with blood concentrations of the various anesthetic agents at different planes of anesthesia. By so doing, they laid a firm foundation for the electroencephalographic monitoring of depth of anesthesia.

Other investigators recognized that the electroencephalogram taken during maintenance of general anesthesia could be affected by certain cortical insults unrelated to the anesthetic agent. Beecher, McDonough, and Forbes[8] described the effects of hypotension during ether anesthesia in 1938. They found that an e of hypotension resulted in electroencephalographic patterns similar tc f deepening anesthesia, although the concentration of administered a was unchanged. In 1950, Goldensohn, Busse, and their co-worke at a similar progression of the electroencephalographic patterns n hypercarbia incident to diffusion respiration during Pentothal The effect of low oxygen tension on the electroencephalogram w y Davis and his associates[10] as early as 1938. In 1953, owes, K urney, and Simeone[11] described the electrocardio- ic eff arbia and anoxia during anesthesia for surgical es.

in the operating room, the electroencephalogram depression. It is recognized that the anesthetic

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., Division of Anesthesiology, University of California

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agents are only one of many factors which may depress the cerebrum during such procedures. When the depression is greater than that expected from the amount of anesthetic agent administered, an additional cause of cerebral depression (anoxia, hypercarbia, decreased cerebral circulation) is assumed to be affecting electrical activity and an effort is made to find the cause and eliminate it.

During the past 2 years, electroencephalographic monitoring has been applied to all open heart procedures (cardiac bypass or hypothermia with occluded circulation) performed at the University of California Hospital, Los Angeles. On five occasions during thoracotomy for cardiac bypass, but before the pumping procedure started, we had noted a depression of cortical electrical activity associated with compression of the superior vena cava. In all cases, the depression was unaccompanied by changes in the electrocardiogram, systemic blood pressure, or respiratory pattern. In Case 1, 2, 3, and 5, the electroencephalographic patterns returned to the predepression pattern shortly after the compression of the superior vena cava was released, and before any changes were made in pulmonary ventilation or concentration of anesthetic gases administered. In the fourth case, the electroencephalographic pattern gradually returned to the predepression level even though the partial occlusion of the superior vena cava was not released.

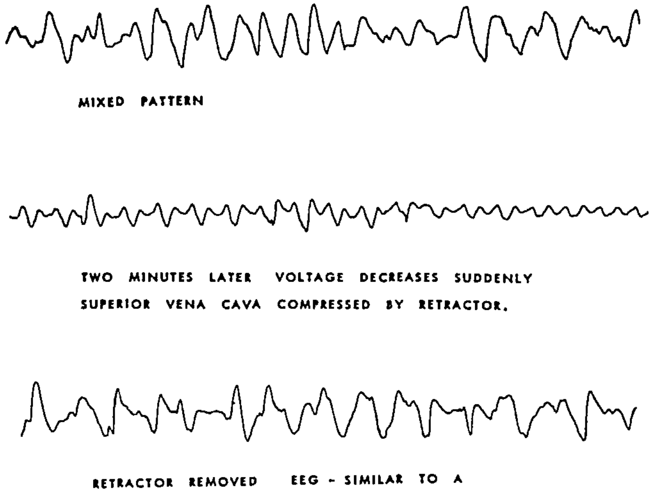


Fig. 1—Thoracotomy under cyclopropane anesthesia. Tracings taken after pleura opened.

Cyclopropane was used as an anesthetic agent in all cases. The 5 cases are presented below.

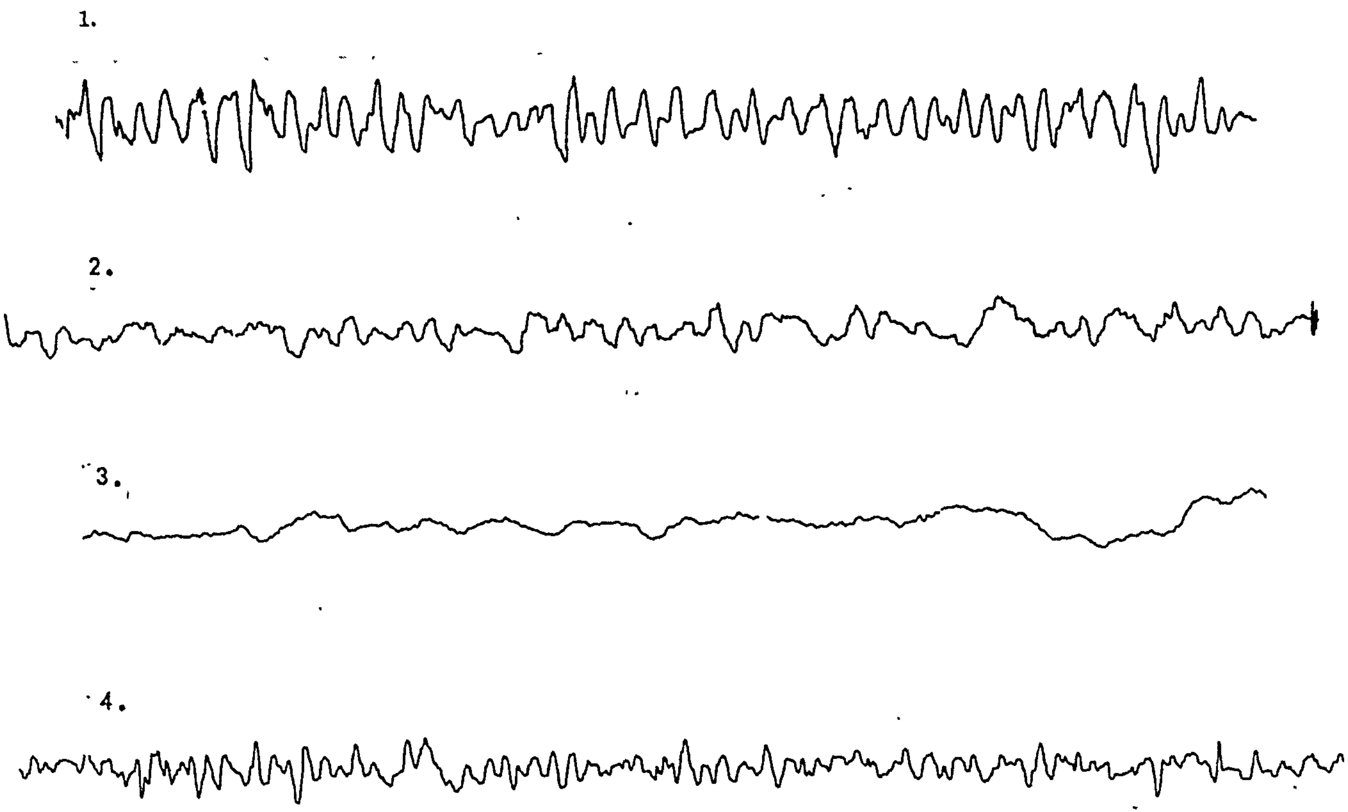


Fig. 2.—*1*, EEG prior to obstruction of superior vena cava. *2*, Appearance of moderately severe depression *3*, Appearance of severe depression. Obstruction of superior vena cava found and released. *4*, Approximately 2 minutes after cava released. EEG similar to Tracing *1*.

Case 1 (Fig 1) —The operative procedure and maintenance of anesthesia was uncomplicated until the voltage of the electroencephalographic patterns decreased over a 2 minute period This was unaccompanied by any change in frequency of cortical activity Pulse rate, blood pressure, and the electrocardiographic patterns were unchanged The surgeon was notified of the alteration and noted that a retractor was partially occluding the superior vena cava The retractor was removed and the voltage promptly returned to the predepression level

Case 2 (Fig 2) —The electroencephalographic pattern developed a sudden decrease in voltage with slowing in frequency These changes rapidly progressed to complete cortical electrical silence A retractor was found compressing the superior vena cava The electrical activity of the brain rapidly returned to the predepression level when the retractor was removed The concentration of cyclopropane was not changed during this episode

Case 3 (Fig 3) —The electroencephalographic tracings were being recorded at a slow paper speed of 1 mm per second An increase in voltage was noted and the paper speed was increased to 15 mm per second A pattern of moderately severe cortical depression developed and it was noted that the superior vena cava was partially obstructed by a clamp The obstruction was removed and the cortical electrical activity rapidly changed to a faster frequency and lower voltage

Case 4 (Fig 4) —As the great vessels were being freed, the surgeon stated that in order to get proper exposure, it was necessary to retract the superior vena cava to such a degree that it would be partially occluded Prior to partial occlusion, the electroencephalographic pattern was one of fast frequency (18 to 20 c p s) at relatively low voltage (less than 100 microvolts), 20 seconds following partial occlusion, the frequency slowed and the voltage increased until a pattern of moderate depression was established The cortical electrical activity showed no further depression during the next 2 minutes Then, even though the superior vena cava remained partially occluded, the cortical electrical activity returned to the predepression level

Case 5 (Fig 5) —Difficulty was encountered during insertion of a drainage catheter into the superior vena cava prior to the pumping procedure On the basis of experience from the preceding 4 cases, the surgeon requested that the electroencephalogram be closely observed Coincident with this request it was noted that the electroencephalographic pattern was changing from 6 to 8 c p s frequency and voltage to 100 μv to a pattern of slow frequency (1 to 2 c p s) high voltage (200 to 300 μv), thus reflecting a moderately severe degree of cortical depression The cortical depression continued to increase over the next 20 seconds until a pattern of electrical silence was recorded The electrical silence persisted during the next 3 minutes while the surgeon attempted to readjust the position of the catheter The catheter was then removed This was followed by a rapid return of the electrical cortical activity (low voltage 6 c p s activity) A smaller catheter was then inserted into the superior vena cava without any accompanying electroencephalographic change

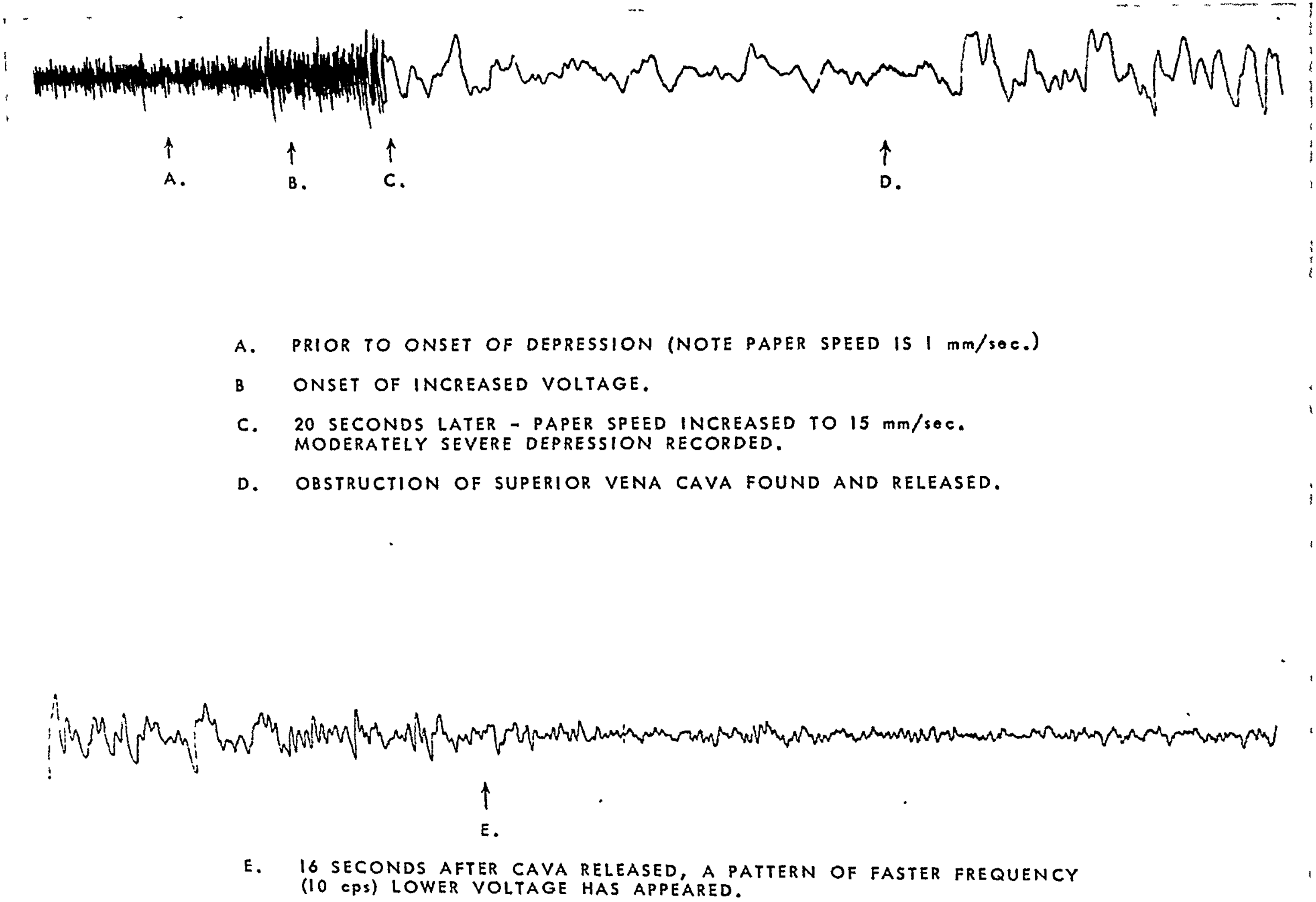
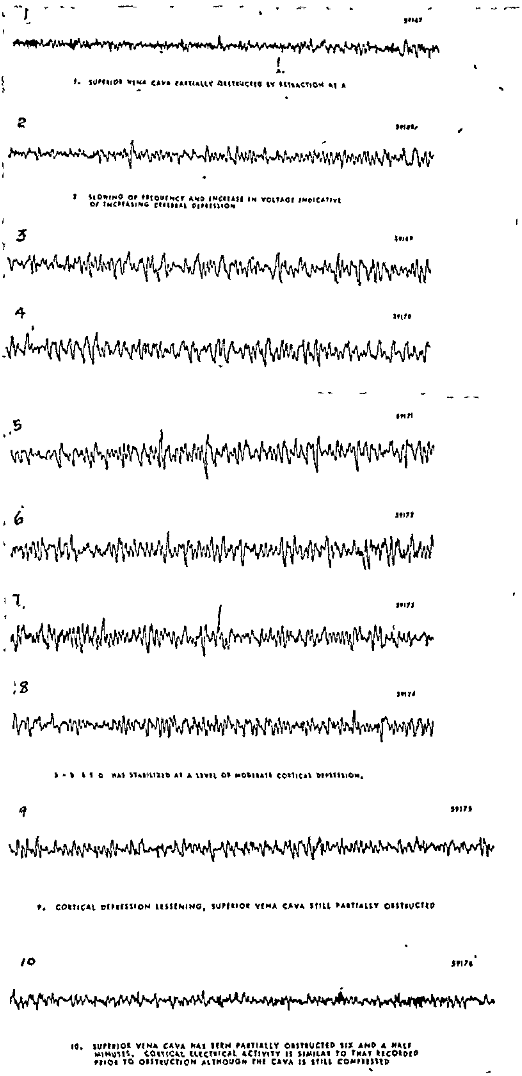


Fig. 3.—Continuous tracing.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1. SUPERIOR VENA CAVA PARTIALLY OBSTRUCTED BY RETRACTION AT A
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2 SLOWING OF FREQUENCY AND INCREASE IN VOLTAGE INDICATIVE OF INCREASING CEREBRAL DEPRESSION
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3 - 8 E E G HAS STABILIZED AT A LEVEL OF MODERATE CORTICAL DEPRESSION.
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9. CORTICAL DEPRESSION LESSENING, SUPERIOR VENA CAVA STILL PARTIALLY OBSTRUCTED
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10. SUPERIOR VENA CAVA HAS BEEN PARTIALLY OBSTRUCTED SIX AND A HALF MINUTES. CORTICAL ELECTRICAL ACTIVITY IS SIMILAR TO THAT RECORDED PRIOR TO OBSTRUCTION ALTHOUGH THE CAVA IS STILL COMPRESSED

Fig. 4.—Continuous tracing. *1,* Superior vena cava partially obstructed by retraction at *A*. *2,* Slowing of frequency and increase in voltage indicative of increasing cerebral depression. *3—8,* EEG has stabilized at [illegible] al depression. *9,* Cortical depression lessening, superior vena cava [illegible] *10,* Superior vena cava has been partially obstructed 6½ minutes. [illegible] is similar to that recorded prior to obstruction although the cava is [illegible]

Throughout this episode, all vital signs remained unchanged. Both lungs were visible and well ventilated, and the concentration of cyclopropane administered was [illegible]ed.

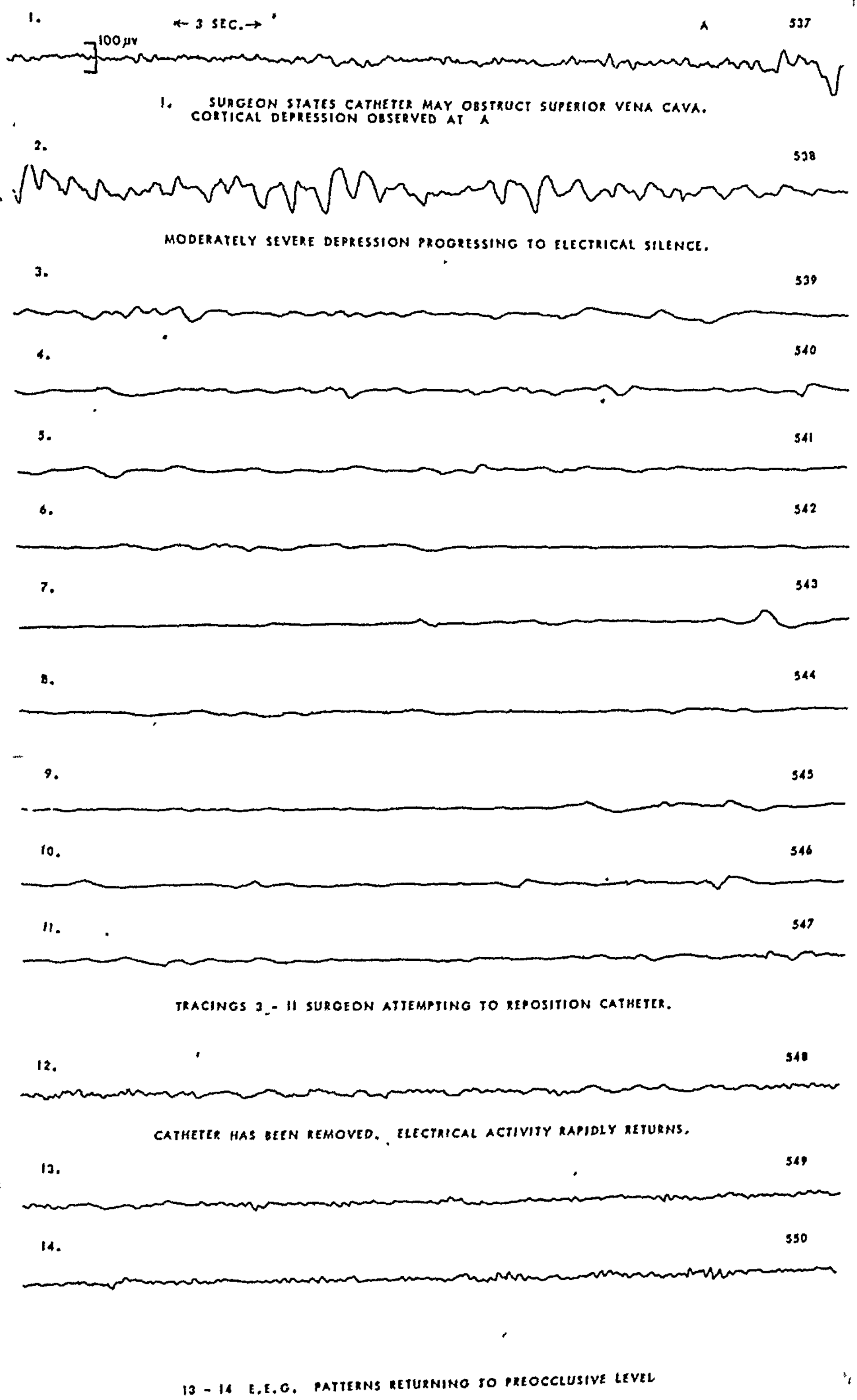

Fig. 5.—Continuous tracing.

DISCUSSION

In Case 4 the superior vena cava was partially obstructed purposely, and the degree of cortical depression monitored electroencephalographically The return of electrical activity to predepression levels while the compression of the superior vena cava persisted may indicate that compensatory mechanisms adjust to the abnormal condition caused by the obstruction The progression of cortical depression to complete electrical silence in Cases 3 and 5 would indicate that these compensatory mechanisms cannot always adjust satisfactorily

Although the venous pressure in the internal jugular vein was not measured in any of these patients, it seemed possible that the electroencephalographic depression associated with obstruction of the superior vena cava results from increased cerebral venous pressure In all cases we were impressed by the absence of change in vital signs electrocardiographic signal, and systemic blood pressure associated with the cortical depression

These observations, as well as others in different types of cases have led us to believe that electroencephalographic monitoring of anesthetized patients constitutes a valuable addition to methods of monitoring the proper conduct of both anesthesia and surgery While it is appreciated that it is not practical to employ all possible methods of monitoring in all surgical patients, these observations would tend to point out that care in the placement of retractors during thoracic surgery may prevent some otherwise unexplained postoperative *neurological sequelae or sequelae that may have been attributed to anesthesia*

SUMMARY

Five cases of depression of cortical electrical activity associated with partial obstruction of the superior vena cava are presented

In the 5 cases presented, the electroencephalographic depression was unassociated with changes in vital signs and electrocardiographic signals Electroencephalographic monitoring allows the early detection of a cerebral insult which might have resulted in cortical damage had it been allowed to persist

It is suggested that the cortical depression described in these 5 cases resulted from increased cerebral venous pressure

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PRACTICAL METHODS OF HOMOLOGOUS CARDIAC TRANSPLANTATION

Watts R. Webb, M.D., Hector S. Howard, M.D., and William A. Neely, M.D.
Jackson, Miss.
With the Technical Assistance of Stennis Wax and Dyke Hagaman

Previous experiments have demonstrated fundamental principles of transplantation of the heart with both lungs, and the heart with one lung.[1] Homologous or autologous transplantation of the heart with both lungs is feasible technically, but encounters the physiologic impasse of respiratory insufficiency, which can be circumvented by leaving one innervated lung in the recipient. While transplantation of the heart with the left lung is technically difficult, due to the overlying arch of the aorta, transplantation of the heart with the right lung (Fig. 1) has proved relatively easy.

These experiments have been continued to develop methods of transplanting the heart by itself, which conceivably could prove more desirable in many circumstances. The heart can survive without circulation for periods of at least 90 minutes at room temperature if, as suggested by Crowell and Smith,[3] the heart is heavily heparinized, or if the blood is perfused from the cardiac capillary bed to prevent the formation of obstructing clots within the coronary vascular bed.[4] If, in addition, the heart is refrigerated in a nutrient medium at 4° C., it can be preserved for at least 6 to 8 hours and return to normal function.[5] Utilizing these methods to gain requisite time and the pump oxygenator to maintain the recipient during the period of transfer, techniques of complete homologous cardiac transplantation have been developed.

METHODS

Matched pairs of healthy adult mongrel dogs were anesthetized with pentobarbital and respirations were maintained by intermittent positive pressure with room air. Sternal splitting incisions were found to offer satisfactory exposure. The dissections in the donor and recipient are comparable except for treatment of the vessels. Preparation of the hearts requires isolation of the inferior and superior venae cavae, aorta, pulmonary artery, and pulmonary veins. The Sondergaard technique was utilized bilaterally to obtain sufficient length for the pulmonary veins, particularly for the left superior pulmonary vein which bifurcates immediately into two small vessels.

From the Department of Surgery, University of Mississippi School of Medicine, Jackson, Miss.

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After inflow occlusion, the donor heart was perfused with lactated Ringer's solution through the right atrium, to flush all blood from the heart and lungs. Alternately, 10 mg. of heparin per kilogram of body weight may be injected intravenously to prevent intravascular clotting during the period of ischemia. After division of the vessels, the heart was dissected free from the trachea to which it is attached by thin areolar tissue, and refrigerated in cold Tyrode's solution containing 10 per cent serum, according to the formula of Gross and co-workers.[6] After the heart had been cooled, couples (Fig. 3) were inserted into the venae cavae and pulmonary veins.

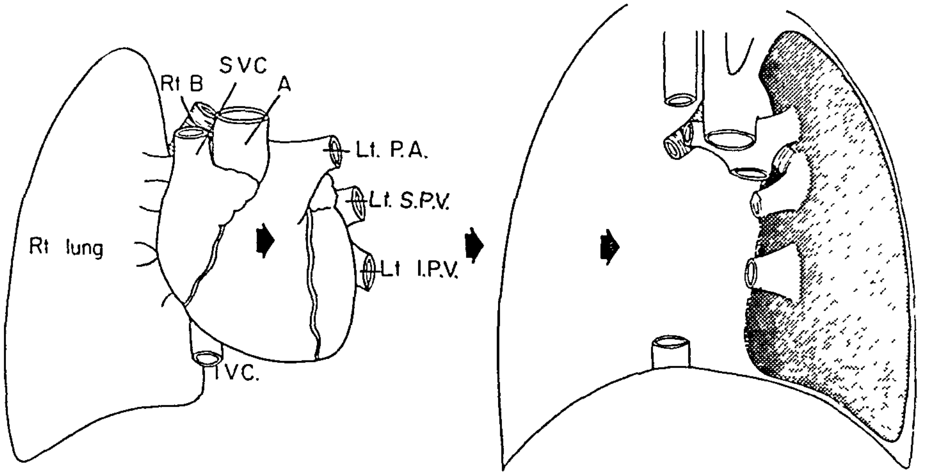

Fig. 1.—Diagram showing anastomoses used in transplantation of heart and right lung.

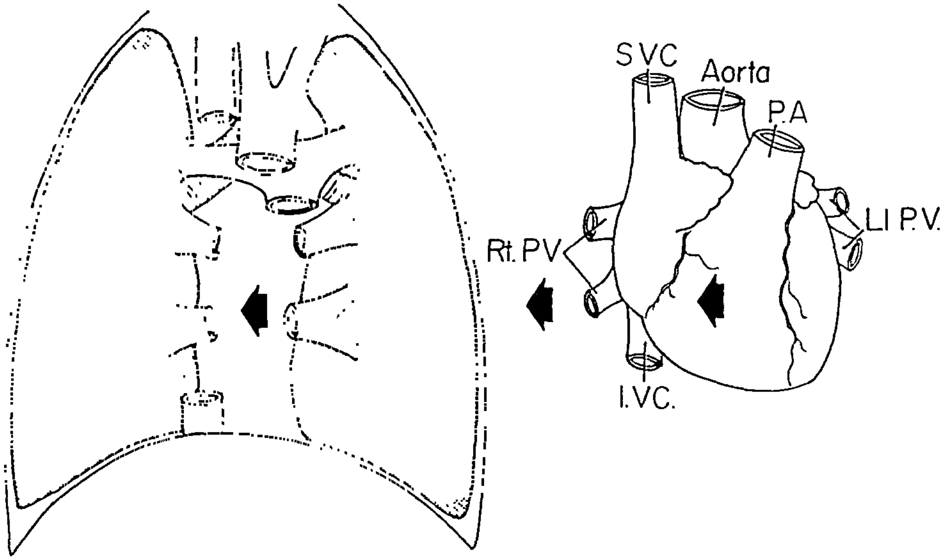

Fig. 2.—Diagram showing anastomoses required in cardiac transplantation.

In the recipient animal, the phrenic nerves were carefully freed from the pericardium, and dissection performed as above. All vessels were left long and, to obtain additional length, the pulmonary veins may be divided with a cuff of atrium. After the preparatory dissection had been completed, the pump-oxygenator was connected by venous catheters inserted in the femoral and jugular veins, and an inflow catheter in a femoral artery. The venae cavae and aorta were cross-clamped and the heart excised

The donor heart was inserted with the venous couples being attached to the corresponding veins. During this period there is some loss of blood through the pulmonary veins due to the bronchial circulation to the lung. After anastomosis of the pulmonary veins to the heart, the inflow from these fill the heart, to aid in preventing air embolism. The pulmonary artery was anastomosed next, and the aorta last. Prior to completion of the aortic anastomosis, a small catheter was inserted into the left ventricle and saline solution injected to remove any remaining air. The aortic clamp was removed first to allow restoration of coronary circulation before the heart assumed the load of the full cardiac output. If a heart had not been refrigerated, the aorta would be anastomosed first to re-establish the coronary circulation as soon as possible.

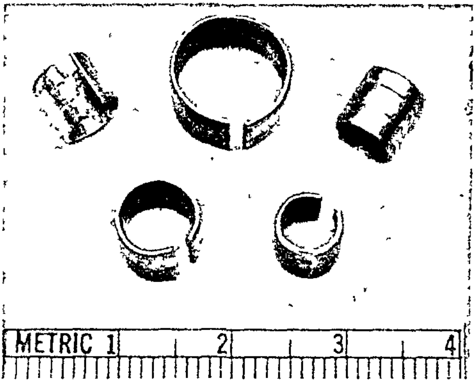

Fig 3—Couples used for venous anastomoses The slit allows easy placement and removal over the vein without allowing leakage

OBSERVATIONS

The donor hearts were exteriorized from 2 to 4 hours before their coronary circulation and function were restored. If the aorta and pulmonary artery were sutured, the actual insertion required about 40 minutes. If, as was occasionally done, the aorta and pulmonary artery were joined with couples, the insertion time could be reduced to about 22 minutes. Usually an additional 20 to 30 minutes and partial support by the pump-oxygenator was required before the transplanted heart was fully warmed and functioning strongly enough to assume the full resting circulatory load.

Countless mistakes and failures were encountered during the developmental phases of this procedure. Of twelve technically successful transplants, however, satisfactory cardiac function with normal blood pressure was restored in ten. Two were lost from arrhythmias and failure. In both of these, air embolism was noted which was thought to be the primary cause of failure. Four hearts spontaneously resumed a sinus rhythm. The remainder fibrillated, but responded to electrical defibrillation. One heart, which had done well for 25 minutes, was lost when additional calcium chloride caused fibrillation which could not be corrected. It was noted repeatedly that these hearts are extremely sensitive to the action of drugs such as calcium or Adrenalin.

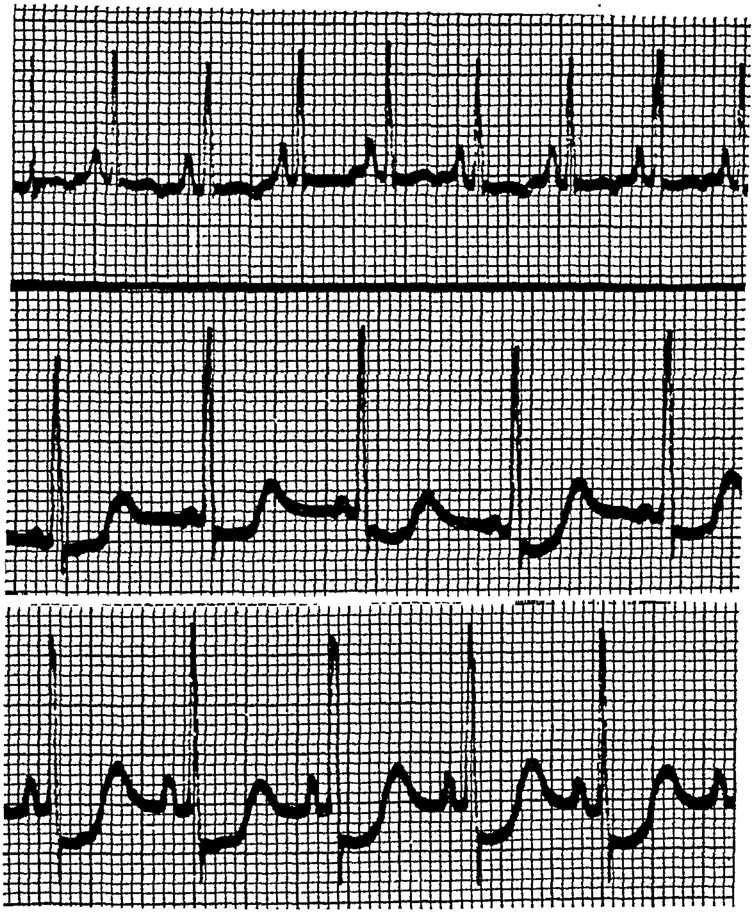

Fig. 4.—Electrocardiogram of Dog 10—Control, 1 hour and 5 hours after transplantation (3 and 7 hours after initial removal from donor). Note the slow rate of the denervated heart and the S-T segment depression suggesting anoxia. Dog died of oozing at 6 hours.

The remaining dogs lived from 30 minutes to 7 hours and 30 minutes. Two dogs showed gradual development of firm, raised, ischemic appearing areas over the surface of the myocardium, suggesting edema of the myocardium, probably from the trauma of massaging the chilled heart. Unfortunately, the pericardium had to be removed during the dissection and most hearts showed small areas of ecchymosis at the areas of greatest trauma from the cardiac massage. These had not been seen with different techniques of transplantation where the pericardium could be preserved. The greatest hazard was continued oozing from the tremendous raw surfaces developed during the procedure. Undoubtedly many of these dogs had developed a hemorrhagic diathesis during the 1- to 2-hour period of cardiopulmonary bypass.

In contrast to those with transplantation of the heart and both lungs, the longer survivors were able to breathe spontaneously. Electrocardiograms (Fig. 4) revealed restoration of relatively normal patterns, the rate was slower as expected in a denervated heart, and most showed S-T segment depression suggestive of the effects of anoxia.

DISCUSSION

Mann and his associates first transplanted puppy hearts into the neck of recipient animals using speed primarily to prevent degeneration of the transplanted heart. They could accomplish the transplantation in 5 minutes, and the puppy hearts survived for several days. Marcus, Wong, and Lusida[8] reported the use of interim perfusion of the donor heart while transplanting it and the lungs into the abdominal cavities of dogs, with anastomoses to the inferior vena cava and the aorta. With artificial respiration, this heart-lung preparation was able to maintain life temporarily while the recipient's own heart and lungs were excluded from the circulation. Neptune and his associates[9] were the first to transplant the combined heart and lungs into the mediastinum to replace the recipient's own heart and lungs, and reported one 6 hour survival. We have *been unable to confirm their finding that such a preparation is compatible with* adequate spontaneous respiration. Our experiences with autotransplantations of the heart and lungs demonstrated that, if the trachea is sectioned at the carina to leave a well innervated trachea, spontaneous return of respiration is possible although the respiration is quite slow and the protective cough reflex is abolished. These latter experiments were performed utilizing the method of Sen, Shah, and Satoskar,[10] who demonstrated continuous recirculation of blood through this isolated heart lung during the transfer.

Berman and his associates[11] have likewise successfully transplanted the heart in dogs with survivals for 21 and 117 minutes. In neither of these, however, was a normal blood pressure developed. Requisite time was gained by the utilization of two teams, so that the heart was out of the body approximately 30 minutes. Rather than utilizing individual anastomoses of the pulmonary veins, the atria were sutured on each side, reducing the number of anastomoses from eight to six.

In view of the numerous anastomoses required, couples of some nature are advantageous. Couples such as those of Fryfogle[12] allow early restoration of blood flow, and the anastomoses can then be performed at leisure. The couples we have used (modified Blakemore tubes) were found to be very similar to those of De Villegas,[13] although developed independently and used somewhat differently. A sewing machine or a stapler such as that devised by the Russian, Androsov,[14] may prove to be extremely valuable.

The above methods outline the general principles for solution of the problems of time and of technique for possible future clinical cardiac transplantation

Obviously, many refinements and further developments are necessary in many phases of this complex procedure before such will be possible. In addition, the unsolved problem of the immunologic responses will prevent permanent survival of any transplanted homologous organ at this time. However, the inroads made by the investigations of Billingham,[15] Enneking,[16] Edgerton,[17] Varco,[18] and many others, point to the general nature of this reaction, and indicate that these problems likewise may be solved.

SUMMARY

Technical and physiologic considerations of free homologous cardiac transplantations are presented. Of twelve technically successful transplants utilizing refrigerated hearts, ten were able to maintain normal blood pressures from 30 minutes to 7½ hours.

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THE BACTERIAL FLORA OF THE HUMAN TRACHEOBRONCHIAL TREE

Noble O. Correll, Jr., M.D., Kenneth C. Johnston, M.D., Hiram T. Langston, M.D., and Ralph H. Hubble, Ph.D., Chicago, Ill.

INTRODUCTION

As the number and extent of operations upon the pulmonary system increases, knowledge of its physiology becomes more important. Studies of the bacterial flora of the tracheobronchial tree would seem to be of value.

METHODS

The bronchial mucus from each of 200 patients in a tuberculosis sanitarium was cultured. The specimens of mucus were obtained at bronchoscopy from 100 patients, and from the open bronchial stump at the time of pulmonary resection from the other 100 patients.

The method for obtaining bronchial mucus at bronchoscopy was as follows: Following production of topical anesthesia with 2 per cent Pontocaine spray of the pharynx and the perlaryngeal instillation of 10 per cent cocaine intratracheally, the patients were bronchoscoped to determine the status of the tracheobronchial tree. During bronchoscopy, a swab was taken of the bronchial mucus from within the main-stem bronchi. The swabs were placed in a sterile container and given to the bacteriologist, who transferred the swabs to trypticase soy broth and incubated them overnight. The broth cultures were examined microscopically after 16 hours of incubation. If the flora appeared to consist of staphylococci, streptococci, pneumococci or any combination of gram-positive cocci, mixed culture sensitivities were made on blood agar and Mueller-Hinton media for a range of antibiotics and sulfonamides. The high-low concentrations of drugs in commercially prepared disks* were used. If gram-negative bacilli were present, isolation on EMB agar was made for further identification and sensitivities.

The method for obtaining bronchial mucus at surgery was as follows: The swabs of bronchial mucus obtained at surgery were made by swirling the sterile cotton applicator in the aggregate of mucus found in the op

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From the Departments of Surgery, University of Illinois College of Medicine and The Chicago State Tuberculosis Sanitarium, Chicago, Ill

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*Bacto-sensitivity disks, Difco Laboratories, Detroit, Mich proximal bronchial opening following transection of the bronchus at the time of pulmonary resection. This collection of mucus was cultured and then smeared for gram stain. With two exceptions, the culture of these swabs began immediately after their receipt from surgery. Invariably these swabs were found to be saturated with blood-tinged mucus. Using aseptic technique, they were swirled in trypticase soy broth, thioglycollate broth, then streaked on blood agar, and finally smeared on a microscopic slide for direct examination by gram stain. Subculture sensitivity studies were made as described previously for cultures from bronchoscopy swabs.

All cultures were continuously incubated at 37° C. until positive or for 4 days if negative. Concurrent incubation under 10 per cent carbon dioxide environment was performed with a limited number of surgical swab specimens. No additional positive cultures were obtained under carbon dioxide.

Of the one hundred resections, there were fifty-seven lobectomies, seventeen pneumonectomies, sixteen segmentectomies, and ten lobectomies with segmentectomies.

RESULTS

All cultures of bronchial mucus obtained at bronchoscopy were positive. Most were mixed cultures and revealed bacteria commonly found in the pharynx. The relative incidence of each microorganism can be seen in Table I.

TABLE I. RESULTS OF CULTURE OF BRONCHIAL MUCUS OBTAINED AT BRONCHOSCOPY

BACTERIA	NO. OF SPECIMENS IN WHICH FOUND
Staphylococcus albus, coagulase negative	40
Staphylococcus albus, coagulase positive	21
Staphylococcus aureus, coagulase negative	15
Staphylococcus aureus, coagulase positive	10
Alpha streptococcus	28
Beta streptococcus	8
Diplococcus pneumoniae	9
Neisseria catarrhalis	4
Aerobacter aerogenes	3
Pseudomonas aeruginosa	1
Proteus vulgaris	1

The cultures of bronchial swabs taken at surgery showed "no growth" in 80 of the 100 cases. The bronchial mucus of 20 patients (20 per cent) contained viable bacteria, usually in pure culture, as shown in Table II.

TABLE II. RESULTS OF CULTURE OF BRONCHIAL MUCUS OBTAINED FROM THE OPEN BRONCHIAL STUMP AT THORACOTOMY

BACTERIA	NO. OF SPECIMENS IN WHICH FOUND
Staphylococcus aureus, coagulase positive	5
Staphylococcus albus, coagulase positive	3
Staphylococcus albus, coagulase negative	3
Alpha streptococcus	4
Diphtheroids	5
Aerobacter aerogenes	1
Bacillus subtilis	1
Paracolon bacillus	1

Of the organisms found from the bronchial mucus taken at bronchoscopy, Table III shows the relative effectiveness of the different antibacterial agents.

TABLE III. RESULTS OF SENSITIVITY STUDIES ON BACTERIA IN BRONCHIAL MUCUS OBTAINED AT BRONCHOSCOPY

ANTIBIOTIC OR AGENT	% HIGHLY SENSITIVE	% MODERATELY SENSITIVE	% RESISTANT
Chloromycetin	90	8	2
Magnamycin	88	5	7
Erythromycin	85	8	7
Novobiocin	85	10	5
Aureomycin	73	18	9
Terramycin	65	11	24
Tetracycline	62	17	21
Penicillin	66	10	24
Streptomycin	25	15	60
Gantrisin	9	28	63
Sulfadiazine	7	23	70

Of the organisms recovered from the open bronchial stumps at surgery Table IV shows the relative effectiveness of the different antibacterial agents.

TABLE IV. RESULTS OF SENSITIVITY STUDIES ON BACTERIA IN BRONCHIAL MUCUS OBTAINED FROM THE OPEN BRONCHIAL STUMP AT THORACOTOMY

ANTIBIOTIC OR AGENT	% HIGHLY SENSITIVE	% MODERATELY SENSITIVE	% RESISTANT
Chloromycetin	88	0	12
Magnamycin	65	10	25
Erythromycin	75	0	25
Novobiocin	70	15	15
Aureomycin	88	0	12
Terramycin	75	0	25
Tetracycline	75	10	15
Penicillin	55	10	35
Streptomycin	60	30	10
Gantrisin	15	30	55
Sulfadiazine	10	35	55

DISCUSSION

From these data it is obvious that the bacterial content of bronchial mucus differs, depending upon how it is collected. Those specimens of bronchial mucus obtained at bronchoscopy uniformly grew bacteria, usually in mixed culture, whereas the mucus obtained through the open bronchial stump at surgery was sterile in 80 per cent of the 100 cases studied.

It is suggested that the high incidence of positive cultures from the bronchoscopic specimens is due to the aspiration of saliva, high in bacterial content, into the normally sterile tracheobronchial tree. Such aspiration surely occurs as the result of reflex coughing initiated by the intratracheal instillation of the topical anesthetic agent. The possibility of pharyngeal mucus contaminating the bronchoscope during its passage is also to be considered, although inserting the sterile bronchoscope directly into the trachea through a sterile laryngoscope still provided mucus which grew bacteria upon culture.

It is possible that some of the positive cultures obtained from bronchial secretions taken from the open bronchial stump at surgery were the result of contamination from the anesthetist's aspirating catheter during the practice of performing tracheobronchial toilet. This factor seems especially likely in at least two instances in our series in which the anesthetist had to do multiple tracheal aspirations and manipulate the endotracheal tube to resposition it during the operation.

The remaining 18 surgical patients, found to have bacteria in their bronchial mucus, showed a high incidence of other complicating factors: 5 had sputum positive for tubercle bacillus on smear of sputum preoperatively; 3 had bronchogenic carcinoma; 2 had bronchopleural fistulas preoperatively; one had hemopneumothorax preoperatively, and one had an unusual bronchial anomaly.

The remaining 7 patients with bacteria in the bronchial mucus had no known complicating factors. Their organisms were: two hemolytic *Staphylococcus aureus;* three diphtheroids; one alpha streptococcus and two *Staphylococcus albus.*

There was no correlation between the level at which the mucus was acquired and the presence of bacteria. There were thirteen positive cultures from the fifty-seven lobar stumps, three positive cultures from the sixteen segmental stumps, two positive cultures from the seventeen pneumonectomy stumps, and two positive cultures from the 10 patients having more than one surgical stump.

SUMMARY AND CONCLUSIONS

1. The normal human tracheobronchial mucus lining is quite likely sterile.

2. Various bronchopulmonary pathologic states favor the presence of microorganisms.

3. Bronchial mucus obtained at bronchoscopy following topical anesthesia is likely to be contaminated, probably by aspirated saliva.

NONOBSTRUCTIVE CONSOLIDATION ATELECTASIS FOLLOWING THORACOTOMY

Morris M. Culiner, M.D., Stanley B. Reich, M.D., and Jacob Abouav, M.D., San Francisco, Calif.

Collapse of the lung, secondary to obstruction by secretions of the tracheobronchial tree, is a common postoperative complication. Collapse of the lung occurring after thoracotomy, without obstruction of the tracheobronchial tree, or massive pleural effusion or hemorrhage, is a very unusual complication.

In 1908, W. Pasteur[1] described cases of massive lung collapse, and defined this as "total deflation of a large area of lung tissue of sudden onset—in the absence of any signs of obstruction of the airway or of any known cause of compression—due to failure of inspiratory power." He referred to cases of postdiphtheric paralysis of the diaphragm and occasionally of the intercostal muscles and felt that the distending force on the lungs became less than the elastic and muscular agencies which tend to cause its contraction, and so the affected portion of the lung rapidly empties itself of contained air.

His evaluation of the patency of the tracheobronchial tree was, of course, largely on the basis of physical examination, since bronchoscopy was not carried out. This paper initiated controversy and, in 1914, Elliott and Dingley denied the possibility of collapse without bronchial obstruction. In support of this they stated: "The only possible explanation along these lines (collapse without bronchial obstruction) supposes the alveolar wall to have active contractile power like that of muscle, and this assumption finds no ground for its support in the facts of present physiological knowledge." In the light of our present knowledge their tenets and objections are invalid.

Churchill,[3] in a classic paper published in 1925, discussed the etiology of pulmonary collapse and ascribed it to the result of two conditions, in varying degrees of importance in each case: (1) weakened force of respiratory muscle action as in debilitating diseases, myasthenia gravis, and trauma to the chest, accidental or operative, and (2) bronchial obstruction.

He implied that the bronchial obstruction is a much more significant factor in lung collapse. He did, however, discuss a case of pulmonary infarction, with

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From the Departments of Surgery and Radiology, Mount Zion Hospital and Medical Center, San Francisco, Calif.

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severe pleuritic pain, in which case lung collapse subsequently developed. In this patient, he felt that the bronchial obstruction was not a significant factor, but that inhibition by pain of respiratory muscle function was very important in the etiology of collapse.

Thus, we concur in the opinion that postoperative lung collapse, in the vast majority of cases, is due to obstructing secretions in the tracheobronchial tree. Our experiences, however, with several patients who, by bronchoscopic, radiologic, and physical examinations, were proved not to have obstructing tracheobronchial secretions or other obstructing mechanisms have convinced us that the complication of nonobstructive pulmonary consolidation-atelectasis can and does occur. We have also found references in the recent literature to cases of transitory lung collapse occurring postoperatively, without explanation for this collapse being offered. Once the physiologic basis for this complication is appreciated more cases will be recognized.

Without going into detail concerning the dynamics of respiration we will briefly discuss the basic factors responsible for pulmonary aeration.

Aeration of the lung occurs as a passive filling, through a patent tracheobronchial tree, in response to pleuroparenchymal pressure differentials that result from an increase in the volume of the thoracic cage. The volumetric increase is secondary to the active factors of (1) descent of the diaphragm, and (2) elevation of the ribs and the sternum by the other muscles of respiration. Cessation of action of either factor usually can be compensated adequately by the other factor.

Splinting, due to pain, of the respiratory excursion of the thoracic wall is commonly seen in the period following thoracotomy, and may be essentially complete. Phrenic nerve paresis or severance may occasionally occur as a result of the operative dissection. When both inhibition of the thoracic wall excursion and phrenic paralysis follow a thoracotomy, passive lung aeration no longer occurs and the lung collapses as air is absorbed. Under these circumstances, the tracheobronchial tree remains unobstructed.

Summaries of several cases illustrative of this complication are presented.

CASE REPORTS

CASE 1.—V. H., a 59-year-old white woman. This patient was admitted on Jan. 14, 1957, for repair of an esophageal hiatus hernia. On January 15, a transthoracic repair was carried out utilizing a diaphragmatic counter-incision for traction-reduction of the herniated stomach. For several days following operation normal lung aeration was present.

On January 19, there was a marked diminution in breath sounds over the left lower lobe. A roentgenogram made on January 20 (Fig. 1, *A* and *B*) revealed left lower lobe collapse.

On January 21, bronchoscopy was done. No significant amount of secretion was found in the tracheobronchial tree. No improvement in aeration occurred postbronchoscopy.

On January 23, a repeat x-ray film indicated continued collapse of the left lower lobe. Bronchoscopy was repeated. No secretions were present within the tracheobronchial tree. A widely patent left bronchus down to and including all segmental orifices was seen.

On January 26, x-ray (Fig. 1, *C*) and fluoroscopic examinations revealed a fixed left diaphragmatic leaf and almost complete left lung collapse with mediastinal shift to the left. On Feb. 2, 1957, an x-ray film (Fig. 1, *D*) showed complete left lung collapse.

The patient had complained of severe incisional pain during the entire postoperative period On February 4 and 7, intercostal nerve blocks were done to decrease the chest wall pain The patient was instructed in breathing exercises From February 4 to 11, there was spontaneous expansion of the left lung to the point of almost complete aeration with a

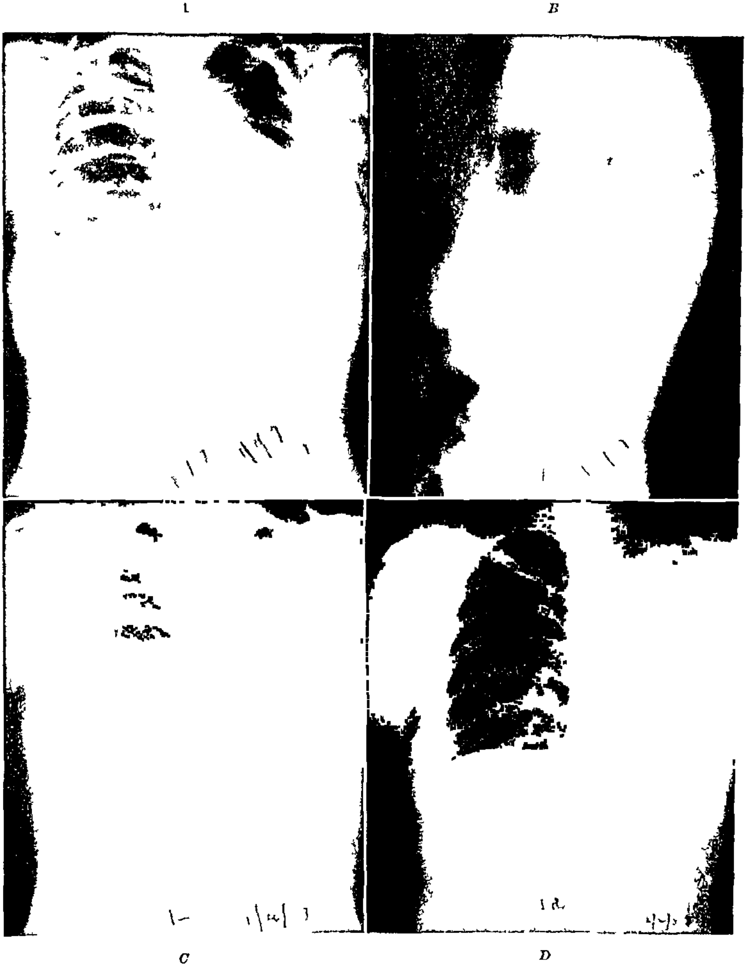


Fig 1 — A and B Roentgenograms made on 1 20 57 showing left lower lobe consolidation atelectasis and mediastinal shift to the left

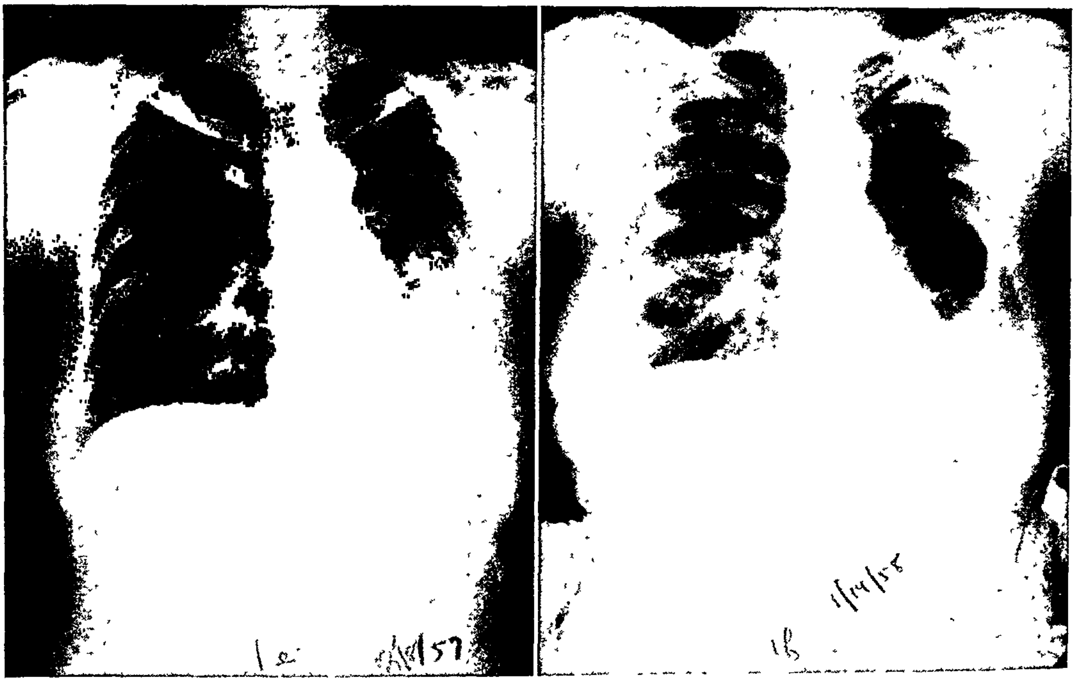
C Posteroanterior view made on 1 26 57 showing almost complete left lung collapse

D Posteroanterior view made on 2 2 57 showing complete left lung collapse and marked mediastinal shift to the left.

return of the mediastinum to normal position. On Feb. 11, 1957, the patient was discharged home. Follow-up x-ray examinations and fluoroscopy were done on Jan. 14, 1958. The films showed complete lung expansion. Fluoroscopy revealed the central paralysis to be permanent; there was some peripheral normal diaphragmatic function.

Comment.—This was our first recognized encounter with this entity and we were at a loss to appreciate fully the factors involved. It was decided on Feb. 4, 1957, to employ intercostal nerve blocks to decrease the pain element and to relieve the chest wall splinting. With improved thoracic wall excursions and despite the permanent phrenic paralysis, spontaneous aeration of the lung occurred.

Lung collapse occurred here in the presence of a patent tracheobronchial tree. The left thoracic wall motion was markedly inhibited by pain. This, in association with the left diaphragmatic leaf paralysis due to the operative procedure, resulted in the two factors responsible for lung aeration being completely nullified.



E. *F.*

Fig. 1.—Cont'd. *E*, Posteroanterior view made on 2-8-57 demonstrating re-aeration to be almost complete and a return of the mediastinal structures to normal midline position.

F, This posteroanterior view made on 1-14-58 shows complete lung aeration. The left leaf of the diaphragm is higher than the right.

Case 2.—D. S., a 5-month-old infant. The second case preceded Case 1 but its complication was never understood at the time of occurrence and only clarified itself in retrospect.

The infant was admitted on Nov. 1, 1954, with a tentative diagnosis of double aortic arch. After preliminary investigation, an exploratory thoracotomy was undertaken. At exploration on November 23, no anomaly was found but the mediastinal dissection was quite extensive.

On November 24, the infant manifested severe respiratory distress. An x-ray film made on November 24 (Fig. 2, A) showed relatively good left lung expansion as well as normal right lung aeration. The degree of respiratory distress decreased but there was some persistence of the respiratory difficulty. The patient was discharged on Dec. 5, 1954, unfortunately without further chest roentgenograms having been taken.

The infant continued to have some respiratory distress at home and repeat x-ray examination on December 15 (Fig. 2, *B*) demonstrated complete opacification of the left hemithorax, with elevation of the left diaphragm, and mediastinal shift to the left.

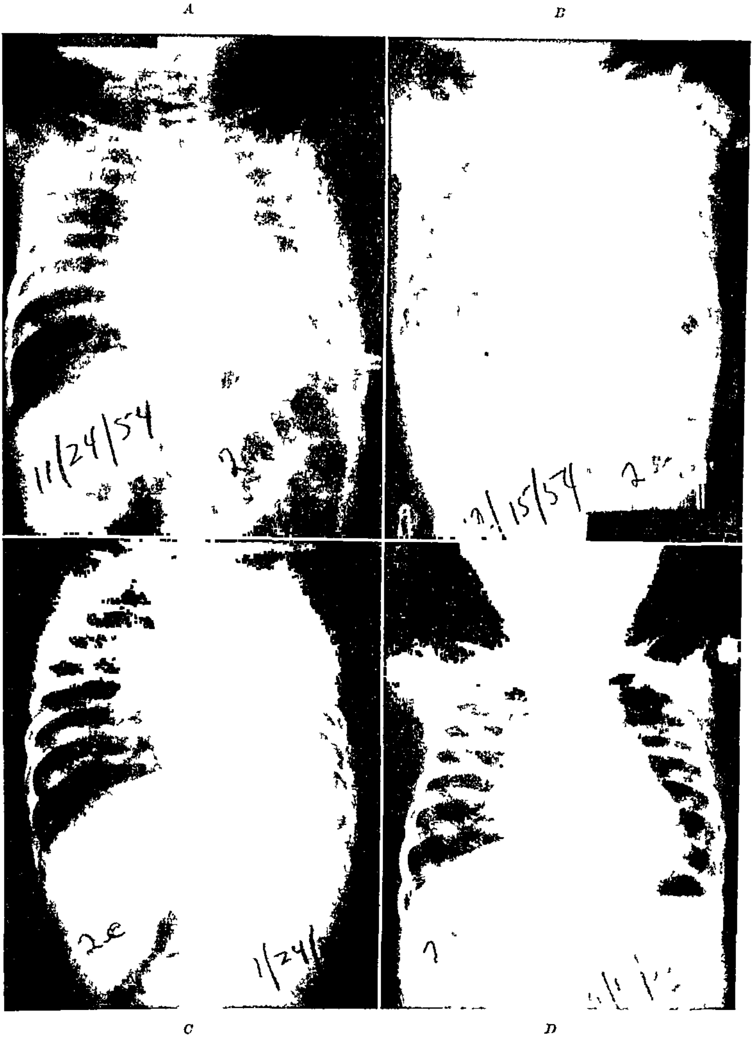


Fig 2—*A* This roentgenogram of 11 24 54 the first postoperative day shows incomplete left lung expansion and aeration The left diaphragmatic leaf is slightly higher than the right

B On 12 15 54 twenty first postoperative day the left hemithorax is completely opaque There is mediastinal shift to the left and elevation of the left diaphragm

C On 1 24 55 2 months postoperative the left lung remains opaque and shows associated mediastinal shift to the left Close view of the original roentgenogram showed the left bronchus to be patent and air containing down to segmental branches

D, This view made on 5 17 57 7 months postoperative demonstrates complete aeration and re expansion of the left lung The mediastinal structures and the left diaphragmatic leaf are in normal position

The patient was readmitted on Jan. 6, 1955, for study. Fluoroscopy on January 7 showed paradoxical movement of the left leaf of the diaphragm and indicated complete paralysis of the left leaf.

Bronchoscopy on January 8 showed no significant amount of secretion in the left main-stem bronchus or trachea and only some edema of the mucosa.

On January 15, bronchoscopy was repeated and showed no secretions plugging the tracheobronchial tree.

Treatment could not be instituted since the cause of the consolidation-atelectasis of the lung with its resultant respiratory difficulty could not be elucidated.

The patient was discharged on Jan. 27, 1955. At home, the patient gradually improved. He was readmitted on Jan. 17, 1955. At this time an x-ray film of the chest (Fig. 2, *D*) showed lung re-expansion and aeration to be complete and a return of the diaphragm to a normal lower level. On Sept. 7, 1956, fluoroscopy revealed normal diaphragmatic motion.

Comment.—This infant demonstrated consolidation-atelectasis secondary to diaphragmatic paralysis. The factor of pain is of much less significance in the infant than in the adult postoperatively in limiting thoracic wall respiratory movement. Respiration in infants is largely a function of diaphragmatic movement, not of thoracic wall movement. The ribs in the infant are nearly horizontal at the end of expiration. Elevation of the ribs during inspiration is of minor degree. Aeration, therefore, is almost entirely a function of diaphragmatic action with very little rib or sternal movement. Thus, this infant showed left lung opacification and no aeration as long as the diaphragm remained without function, and much beyond the period of splinting due to pain following thoracotomy.

CASE 3.—B. R., a 56-year-old white man. This patient demonstrated a coin lesion of the left upper lobe on x-ray examination on Sept. 9, 1957. The x-ray film at that time showed the left diaphragm and the mediastinum to be in normal positions.

On September 11, a left upper lobectomy was done for carcinoma of the lung and the dissection entailed minimal mediastinal manipulation. On x-ray study of September 12 (Fig. 3, *A*), the left diaphragm was markedly elevated and the left lower lobe expansion was incomplete. There was some mediastinal shift to the left.

There was a gradual decrease in respiratory sounds over the left hemithorax to the point of complete absence of vesicular sounds by September 20. The x-ray films at that time (Fig. 3, *B*) showed a completely opaque left hemithorax, further mediastinal shift to the left, and contraction of the hemithorax with continued elevation of the left diaphragmatic leaf. On September 23, fluoroscopy showed an immobile left diaphragmatic leaf. On the same day, bronchoscopy revealed a clear tracheobronchial tree with no mechanical obstruction of the left main-stem bronchus. There was no improvement following bronchoscopy.

Thoracentesis, on Sept. 25, 1957, yielded about 400 c.c. of serosanguineous fluid, certainly insufficient to be responsible to any extent for the complete left chest opacification.

The patient was placed on vigorous breathing exercises at frequent intervals, stress being placed on voluntary left thoracic wall increase of respiratory excursion.

An x-ray examination, on Oct. 5, 1957 (Fig. 3, *C*), showed relatively good lung expansion, although minimal fluid was still present above the left elevated diaphragm. Fluoroscopy and x-ray films, on Jan. 15, 1958 (Fig. 3, *D*), showed good diaphragmatic position and excursion, excellent aeration, and a normal mediastinal position.

Comment.—This case again demonstrated the entity of atelectasis-consolidation resulting from voluntary limitation of thoracic excursion in association with phrenic paralysis. Voluntary respiratory exercises and later return of phrenic nerve function lead to full left lower lobe expansion with descent of the diaphragm and a return of the mediastinum to normal position.

CASE 4.—J. L., a 38-year-old Negro man. On Dec. 18, 1957, this tuberculous patient had a left upper lobectomy and concomitant tailoring thoracoplasty with removal of ribs 2, 3, and 4 and stripping of the undersurface of rib 1. The dissection during lobectomy was exceedingly difficult.

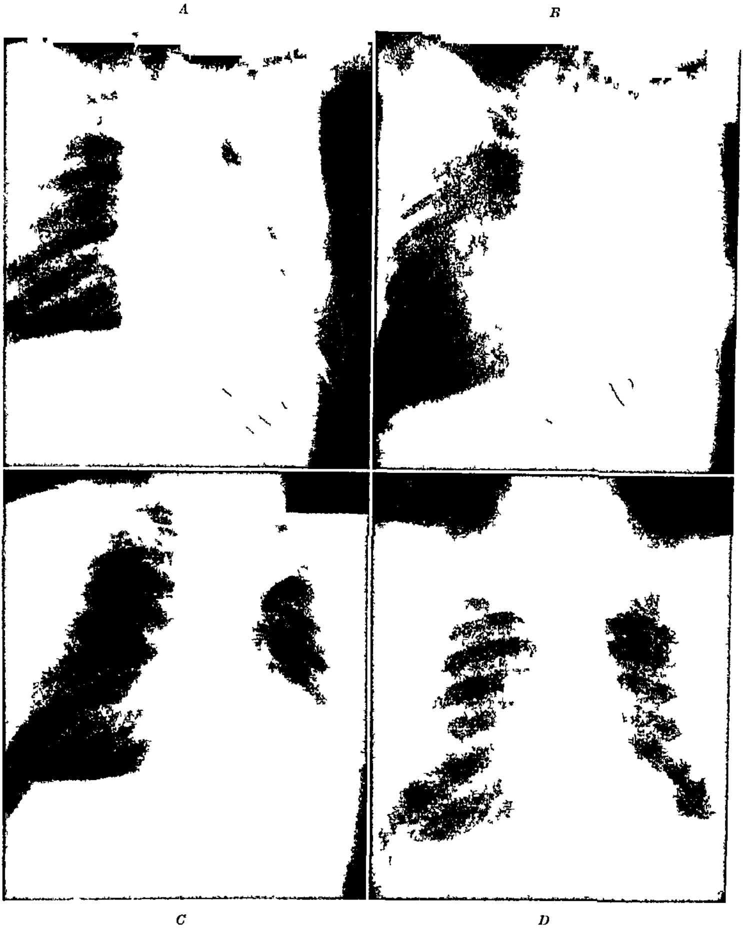


Fig 3 — A This roentgenogram made on 9 12 57 the first postlobectomy day shows incomplete left lower lobe aeration elevation of the left diaphragmatic leaf and marked mediastinal shift to the left

B On 9 20 57 the ninth postoperative day there was complete left lower lobe consolidation atelectasis marked mediastinal displacement to the left, and left diaphragmatic elevation

C, On 10 5 57 left lower lobe re aeration is good and there is partial return of the mediastinal structures to the right

D This view made on 1 15 58 shows excellent left lower lobe expansion and good mediastinal and diaphragmatic position

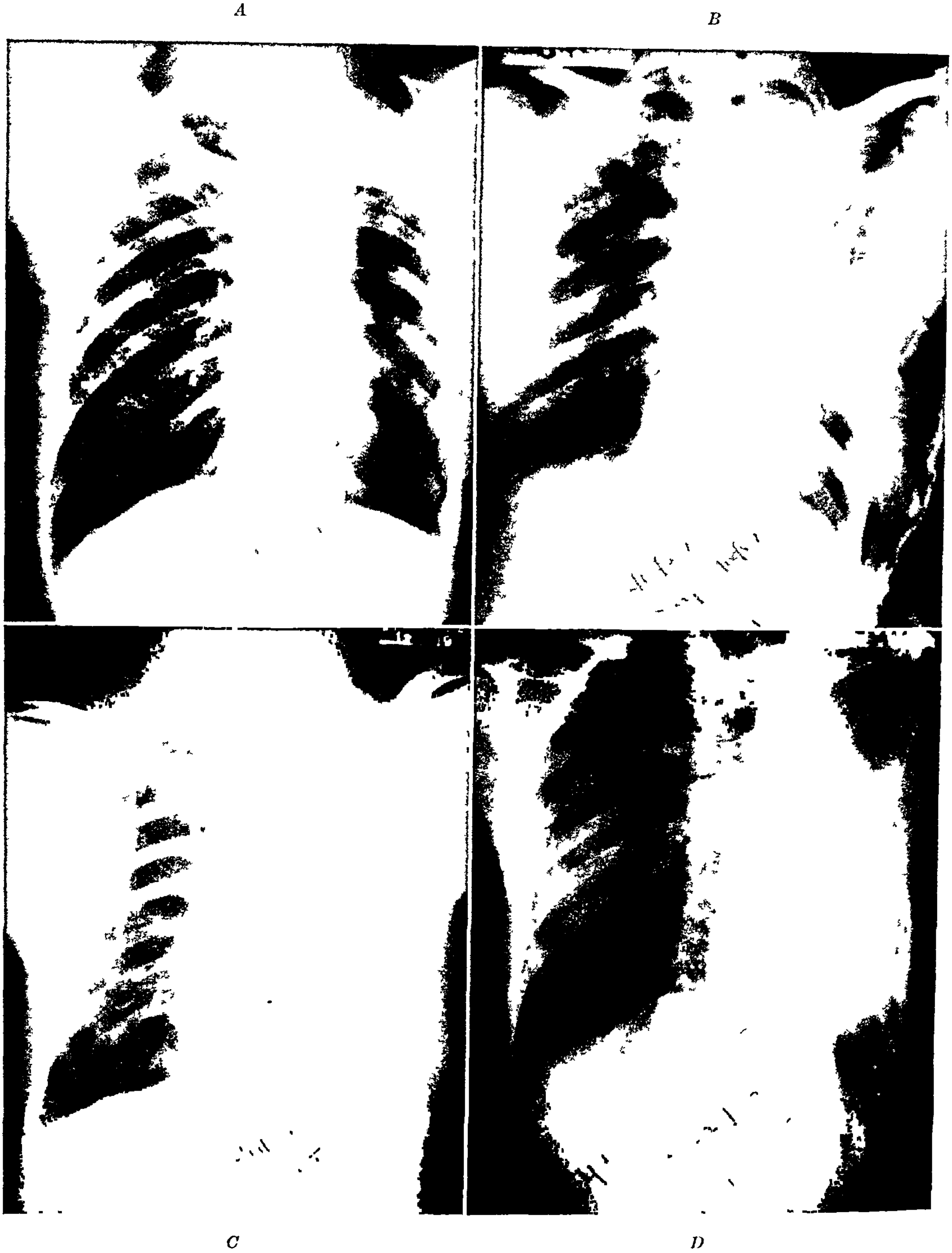


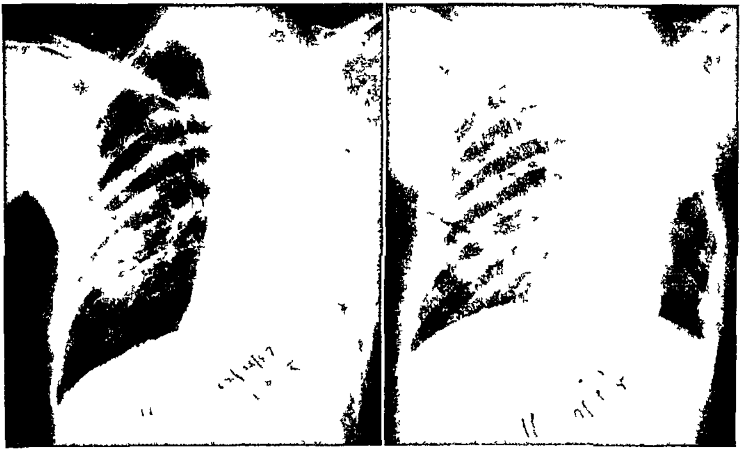
Fig 4.—*A*, This preoperative film of 11-6-57 shows tuberculous fibrocaseous disease of the left upper lobe, normal left diaphragmatic position and slight mediastinal shift to the left

B, This film of 12-18-57, immediately after lobectomy and thoracoplasty, shows relatively good left lower lobe expansion and mediastinal position

C, On 12-19-57, the first day postoperative, lung collapse is complete on the left, and the right heart border is at the left margin of the vertebral column

D, On 12-22-57, the lung was completely collapsed, but the left bronchus and segmental bronchi can be clearly seen to be patent Mediastinal shift to the left is marked

An x-ray film immediately following surgery (Fig 4, *B*) showed aeration of the left lower lobe, and the diaphragm to be in apparently normal position Films of December 19 (Fig 4, *B*) and December 22 (Fig 4, *D*) showed complete opacification on the left The diaphragm cannot be clearly seen The mediastinal shift to the left became more marked Fluoroscopy on the fourth postoperative day, December 22, showed diaphragmatic paralysis on the left, which was confirmed and persistent on Jan 13, 1958, and Feb 23, 1958 The hard film of Dec 22, 1957 (Fig 4, *D*) showed the trachea and the left bronchus to be patent No fluid was present in the pleural space at the time of this film Bronchoscopy, later on this day, yielded very little secretion and the bronchus was widely patent down to and including all segmental orifices No improvement resulted from bronchoscopy Four days later, on the eighth postoperative day, Dec 26, 1957, the left lower lobe showed slight aeration on x-ray examination The x-ray examination of Feb 5, 1958 (Fig 4, *F*), showed excellent left lower lobe expansion, and a return of the mediastinal structures to the right, to their preoperative position



E *F*

Fig 4 —Cont'd *E* On 12 26 57 the ninth postoperative day a little aeration was seen in the left lower lobe

F On 2 5 58 the film shows excellent left lower lobe expansion and aeration and the mediastinal structures are in their preoperative position to the right.

Comment—The phrenic nerve was severed in this case The removal of portions of ribs 2, 3, and 4 and transection of ribs 5 and 6 to permit a fifth interspace approach to the pleural space resulted in postoperative pain, marked splinting, and some paradoxical motion This case demonstrated again consolidation atelectasis following thoracotomy, not due to bronchial obstruction, but due to the loss of function of all the muscles of respiration, diaphragmatic, intercostal and accessory

With a gradual decrease in the splinting of the left chest and an increase in the function of the intercostal muscles in the later postoperative period, spontaneous re-aeration of the left lower lobe followed, despite permanent phrenic nerve loss

DISCUSSION

In the presentation of these 4 cases, we demonstrate an operative complication previously noted but not fully understood We realize [illegible] tion of limited chest wall respiratory excursions in the period following thoracotomy and phrenic paralysis occurs without resulting invariably in total collapse of the ipsilateral remaining lung. The response, however, of any given patient to postoperative pain is an individual variable factor. Whereas all patients after thoracotomy show a decrease in the ipsilateral respiratory excursions, albeit unconsciously, the limitation varies as a voluntary restriction from a minimal to an absolute degree.

The diagnosis of nonobstructive consolidation-atelectasis was established by radiologic and clinical evidence.

1. All cases showed opacification of the hemithorax. It is of interest to note that the collapse occurred, not immediately after thoracotomy, but rather over a period of several days postoperatively. This suggests a slow process resulting from weakness of chest wall excursions with gradual collapse, as opposed to the rapid atelectasis that occurs secondary to bronchial occlusion.

2. Mediastinal shift was to the side of collapse. When spontaneous aeration occurred there was a return of the mediastinum to a more normal midline position in all cases.

3. All patients showed a paralyzed diaphragmatic leaf. The paralysis was temporary in 2 cases, permanent in 2 cases.

4. The patency of the major tracheobronchial tree was established by bronchoscopy in all cases during the period of collapse at a time when maximum opacification was demonstrated by x-ray examination.

Bronchoscopy was done on one or two occasions in each case and, in addition, auscultatory examination of the chest one or more times each day in every case ruled out obstruction by secretions as the basis of collapse of the lung. In addition, the roentgenogram in 2 of these 4 cases showed relatively clearly patent major bronchial and segmental bronchial subdivisions in otherwise opaque collapsed pulmonary tissue.

Certainly, some secretions are always produced by and lie within the minor bronchiolar subdivisions, and thus are beyond our point of vision by bronchoscopy and x-ray examination. To ascribe to these normal secretions obstructing powers is equivalent to stating that the immediate neonatal atelectasis is due to tracheobronchial obstruction by normal tracheobronchial secretions, rather than to the weakness of the inspiratory power of the neonatal muscles of respiration. When the muscles of respiration regained power of action, aeration of the lung occurred, despite the normal minimal secretions of the minor bronchiolar subdivisions.

In our experience, whenever postoperative atelectasis has resulted from obstructing secretions in the tracheobronchial tree, we have never failed to obtain immediate, physically detectable, and easily radiologically demonstrable improvement in lung aeration. In the cases presented in this paper, we obtained no improvement following bronchoscopy and removal of the minimal secretions present in the tracheobronchial tree. It is inconceivable to us that lobar and entire lung collapse can occur secondary to obstruction by secretions, without these secretions being present in the major tracheobronchial tree which is easily visualized by bronchoscopy

Thus, we conclude that these cases represent consolidation atelectasis of a nonobstructive nature, due rather to paralysis of the ipsilateral muscles of respiration, diaphragmatic and intercostal As previously stated, the phrenic paralysis was confirmed in all cases and was permanent in 2, and inhibition by pain of the intercostal muscle action was marked in all but the infant

Therapy must be directed to counterbalancing the factors responsible for the lung collapse The phrenic paralysis cannot be altered We can reduce the voluntary ventilatory restrictions by intercostal nerve blocks, by respiratory exercises, and by the use of an intermittent positive pressure machine We have considered the use of endotracheal intubation and insufflation All these methods will be further investigated

When, in the postoperative period there is a failure of the ipsilateral lung to become or to remain, expanded and obstruction is not present, one might ordinarily consider re-exploration on the assumption that the residual lung collapse resulted from torsion of the pulmonary pedicle or vascular thrombosis That however, should not be done until this syndrome of nonobstructive consolidation atelectasis has been ruled out by bronchoscopy fluoroscopic examination of diaphragmatic action and observation of the degree of respiratory excursion of the ipsilateral thoracic wall

SUMMARY

We present case demonstrations of a complication that follows thoracotomy, resulting from the elimination of the two active factors responsible for pulmonary aeration This complication of lung consolidation atelectasis results from phrenic paralysis in association with restriction by pain of the respiratory excursions of the thoracic wall and despite a clear tracheobronchial tree Therapy has been discussed and further possible methods of treatment suggested

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EMERGENCY THORACOTOMY FOR MASSIVE SPONTANEOUS HEMOPNEUMOTHORAX

John R. Rydell, M.D., Santa Barbara, Calif.

IN RECENT years, several cases have been reported of severe hemorrhage into the pleural space associated with spontaneous pneumothorax. Traditionally it has been well-accepted policy to treat spontaneous pneumothorax in a conservative manner. This has varied from simple observation for the less severe cases, to intermittent needle aspiration or even continuous suction on a cather placed into the intrapleural space. Occasionally intrapleural bleeding wil be associated with spontaneous pneumothorax, but ordinarily this volume of blood loss is not sufficient to cause concern. It is not unusual to aspirate a modest amount of blood at the time of thoracentesis for removal of air. In the past 7 years, sporadic reports have begun to appear in the literature regarding a more aggressive attack on occasional severe cases of hemopneumothorax. It is the purpose of this paper to emphasize the fact that the problem of such bleeding is not always of minor degree. Under certain selected circumstances an emergency thoracotomy may be necessary to stop hemorrhage, which otherwise would continue unabated and finally cause death. Recently, we have treated such a patient, and believe that a policy of earlier operation might have contributed to a more satisfactory result. Wider recognition of the importance of this potentially grave condition may save other lives.

CASE REPORT

The patient, a 55-year-old printer, was admitted to the Cottage Hospital at 6:10 A.M. on Dec. 18, 1957. He had evidently been in good health until about 10 days before his hospital admission, when he developed what he considered to be influenza with mild fever for 2 or 3 days but with a persistent rasping cough since the onset. About 3:00 A.M. on the day of admission, he was awakened by a spell of coughing which was terminated by the occurrence of a widespread pain across the entire precordium, most marked in the left mammary area. He grew progressively more dyspneic following this, and was brought to the hospital with a presumptive diagnosis of an acute coronary occlusion. On examining the patient after hospitalization, it was obvious that the respiration involved a marked lag in the left hemithorax. There was a hyperresonant note to percussion and there were absent breath sounds over the entire left lung. He was ashen gray in color and was perspiring heavily. The blood pressure was 110/70 mm. Hg. The diagnosis was then made of acute pneumothorax and portable x-ray studies confirmed this fact, revealing almost complete collapse of the left lung. There was evidence of pleural fluid at the left base. The mediastinum was shifted to the right side producing considerable compression of the right lung. An electrocardiogram was interpreted as showing a coronary insufficiency pattern.

From the Department of Surgery, Cottage Hospital, Santa Barbara, Calif.

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TABLE I

AUTHOR	DATE	AGE	SEX	PREOPERATIVE CHEST TAPS	TIME OF OPERATION AFTER ONSET	AMOUNT OF BLOOD IN CHEST AT SURGERY (C.C.)	BLEB FORMATION	RESULT
Myers, et al.	1951	22	M	Two; total 1,310 c.c.	60 hr.	2,500	No	Recovered
Ross, C. A.	1952	34	M	Two; total 1,300 c.c.	34 hr.	Large amount	Yes	Recovered
Holloway, et al.	1952	19	M	Four; total 4,100 c.c.	4 days	2,500	No	Recovered
Beatty and Frelick	1953	33	M	Three; total 3,500 c.c.	48 hr.	Large amount	No	Recovered
Beatty and Frelick	1953	21	F	One; total 500 c.c.	48 hr.	1,000	Yes, excised	Recovered
Beatty and Frelick	1953	33	M	One; total 1,900 c.c.	16 hr.	Over 1,000	Yes, excised	Recovered
Ross and Dugan	1953	27	M	Many; over 5,000 c.c.	96 hr.	Full	Yes, excised	Recovered
Borrie	1953	21	M	One; total 1,700 c.c.	24 hr.	2,300	Yes, excised	Recovered
Borrie	1953	26	M	One	24 hr.	1,100	Yes, excised	Recovered
Williams, et al.	1954	33	M	One; total 2,600 c.c.	4 days	1,375	Yes, excised	Recovered
Clyne and Hutter	1955	28	M	One; total 1,140 c.c.	22 hr.	1,140	No source found	Recovered
Clyne and Hutter	1955	32	M	Four; over 1,000 c.c.	6 days	2,300	No; several torn adhesions	Recovered
Agnew	1955	41	M	Six; over 2,000 c.c.	17 days	1,550	No	Recovered
Rydell	1958	56	M	Two; about 1,000 c.c.	30 hr.	2,000	Yes, excised	Died

Usually the pneumothorax is the initiating factor and the hemothorax may not become evident until some days later. Indeed, Powell[1] has stated that some degree of bleeding occurs in 12 per cent of all cases of pneumothorax. Others (Hyde and Hyde), however, have reported a much lower incidence in the range of 3 to 5 per cent. In any event, the frequency of associated bleeding in pneumothorax is high enough and of sufficient danger that it should always be kept in mind as a potentially serious complication. It must be regarded with as much respect as other forms of internal bleeding such as that from peptic ulcer. The same fundamental principles apply to both, namely, that conservatism is proper if the patient can be kept under control by rest, blood transfusions, and other medical therapy, but if the hemorrhage does not soon cease and if the patient shows signs of massive bleeding early surgery must be advised.

Clyne and Hutter[10] have advocated thoracotomy as the treatment of choice for all cases, believing that the risk is less even in the early cases. It is true that convalescence may be prolonged even when the bleeding spontaneously ceases. The clotted blood is often difficult to aspirate from the chest despite the aid of enzymatic débridement and a clotted hemothorax is likely to lead to a failure of the lung to expand. In certain less fortunate cases, it may be necessary to resort to pulmonary decortication to correct an otherwise chronically disabling pulmonary compression.

The similarity of the pathogenesis in most severe instances of hemopneumothorax is remarkable. The source of air escape is usually a ruptured bulla or bleb, which causes the adherent lung to tear small adhesions between the visceral and parietal pleura. These are generally located between the upper lobe and the very apex of the pleural cavity. One should not be lulled into a false sense of security by believing that the bleeding will cease spontaneously since it may originate from the pulmonary vessels with their associated low blood pressure. In nearly all patients operated upon, the bleeding point has been shown to arise from vessels of the systemic circulation, lying in the chest wall under the parietal pleura. It is interesting to observe the massive accumulation of blood which can occur despite a relatively slow ooze from the bleeding point on the parietal pleura. Often electrocoagulation and packing with oxidized cellulose will be sufficient to stop the bleeding. The operation itself should not take long to perform, and many of these patients will improve during the surgery and leave the operating table in much better condition than upon arrival.

Cases have been recently reported in which patients have died of hemorrhage, when thoracotomy with surgical control of the bleeding point would probably have averted such tragedies. When a patient continues to bleed actively for at least 24 hours, it would appear that the safest procedure is to perform thoracotomy. Although it was a bitter disappointment to have the patient die, it must be remembered that he was by far the oldest patient recorded with severe spontaneous hemopneumothorax. It follows that his heart and lungs were less able to withstand the shock of a massive hemorrhage.

SUMMARY

Significant bleeding into the pleural space is associated with spontaneous pneumothorax in from 5 to 10 per cent of cases. The mechanism of the hemorrhage is usually a ruptured bleb or bulla at the apex of the lung. The resulting lung collapse tears pleural adhesions, and starts bleeding from the parietal pleura.

In most instances such bleeding will cease spontaneously with appropriate conservative therapy. Occasionally it will persist and may cause a fatality unless controlled by open thoracotomy. Such a case has been presented.

A plea is made for a more aggressive surgical attack on this problem.

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MASSIVE HEMOTHORAX CAUSED BY AN INTRATHORACIC MENINGOCELE

A Case Report

Hugh E. Wilson, M.D., and Richard W. Ernst, M.D., Dallas, Texas

THE TRIAD of neurofibromatosis, kyphoscoliosis, and intrathoracic meningocele[1-11] has been recognized in the literature. Our purpose is not just to add the thirteenth case to this increasing series, but to underline a heretofore unreported complication of this lesion which would indicate that intrathoracic meningocele is not always a "benign lesion" and that massive hemorrhage may be a constant danger.

CASE REPORT

This 43 year old Negro man arrived at the emergency room of Parkland Memorial Hospital on April 16, 1957, complaining of left anterior chest pain of one day's duration, chills, fever of 100° F., fatigue, and general malaise. During the past few hours he had noted increasing dyspnea.

Past history was essentially noncontributory. The obvious generalized neurofibromatosis and marked kyphoscoliosis of the thoracic spine had been present since early childhood. During a hospital admission 4 years previously for an otitis media, one of the skin lesions was biopsied and the diagnosis confirmed. There was no history of neurological dysfunction.

Physical examination revealed an acutely ill patient; blood pressure 90/70 mm. Hg, pulse 100, respirations 36. There was obvious neurofibromatosis. The left hemithorax was dull to percussion. Breath sounds were absent over the left base and greatly diminish over the apex. There was marked tenderness over the left lower chest wall and the tient complained of increased pain during deep inspiration. Heart sounds were normal. The mediastinum was shifted to the right.

X ray studies of the chest revealed opacity of the left chest and confirm [illegible] shift of the mediastinum to the right (Fig. 1).

Aspiration of the pleural fluid revealed it to be frank blood which did not clot with a hemoglobin concentration of 9 Gm. per cent. The patient's circulating blood hemoglobin was also 9 Gm. per cent. Two thousand and four hundred milliliters of blood were aspirated from the left chest. The patient was transfused with 1,500 ml. of whole blood with prompt improvement. Repeat roentgenograms of the chest revealed a completely re-expanded lung. There remained only a mass in the left vertebral gutter at the level of the lower thoracic spine (Fig. 2).

From the Department of Surgery, The University of Texas Southwestern Medical School, Dallas, Texas.

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Laminagrams in the anterior-posterior and lateral projections were made on April 24, 1957 (Fig. 3). They suggested an extrapleural origin of the tumor. The mass could not be separated from the aorta in either plane. The following differential diagnosis was proposed: (1) aneurysm of the descending thoracic aorta; (2) neurofibroma, intrathoracic, with malignant degeneration; (3) spontaneous hemothorax with encapsulated residual hematoma; (4) the remote possibility of a bronchogenic carcinoma.

Preparation for surgery included making available an aortic graft and a Polyvinyl sponge prosthesis for bypass. The lesion was approached through a left thoracotomy.

Upon opening the chest, fibrinous deposits were noted over the visceral and parietal pleura, especially in the vertebral gutter. The mass consisted of a subpleural meningocele, with a thick fibrinous covering, which protruded into the chest through a vertebral foramen at the hemivertebra. During the early stages of dissection, profuse venous and arterial bleeding came from the vessels tented over the tumor. Before dissection was continued, the center of the mass was aspirated with a needle and clear fluid consistent with spinal fluid was obtained. The vessels, vertebral and intercostals, were so fragile in the organizing hematoma, it was impossible to clamp them. Suture ligatures deep in the adjoining tissue were required for hemostasis. Several of the vessels broke off at the aorta and arterial silk was used to suture the aorta. The meningocele was dissected down to its neck. It was then opened to rule out a myelomeningocele. The spinal cord was seen in the canal but did not protrude into the sac.

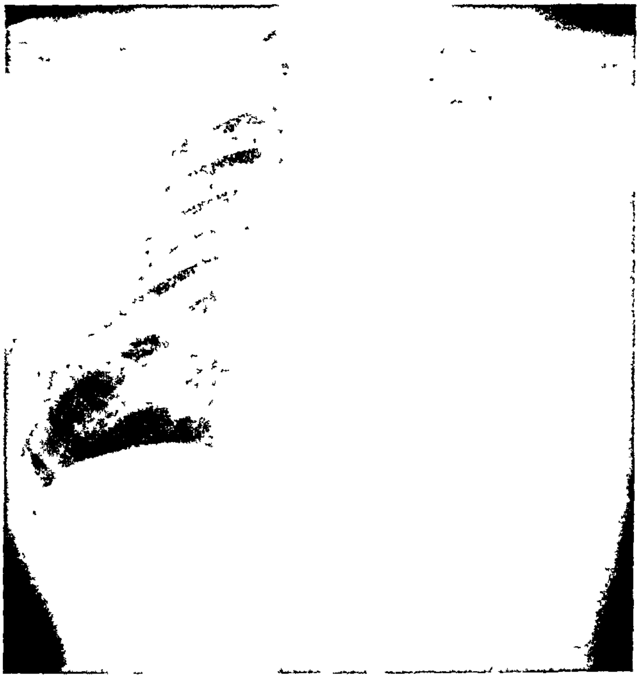


Fig. 1.—Posteroanterior roentgenogram of chest on admission showing massive left hemothorax and shift of mediastinum to the right.

The sac was amputated at the neck, and the neck was closed, top over bottom, with two layers of interrupted silk sutures. No spinal fluid leakage was noted. Hemostasis was completed. The chest was drained to an underwater seal and closed.

The postoperative convalescence was completely uneventful. There was no accumulation of fluid in the chest. The lungs were fully expanded. Repeated examinations, including a 3- and 6-week postoperative follow-up study, revealed no neurological signs of any kind. The patient has resumed full activities.

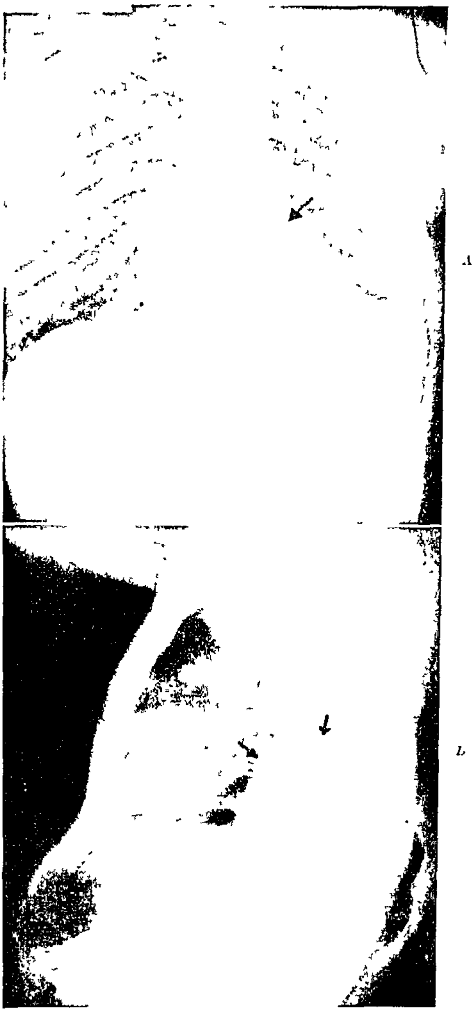


Fig. 2.—*A*, Posteroanterior x-ray of chest after aspiration of blood showing mass in left costal vertebral sulcus behind cardiac silhouette *(arrow)*.

B, Left lateral x-ray of chest showing persistent mass overlying aorta and vertebral bodies *(arrows)*.

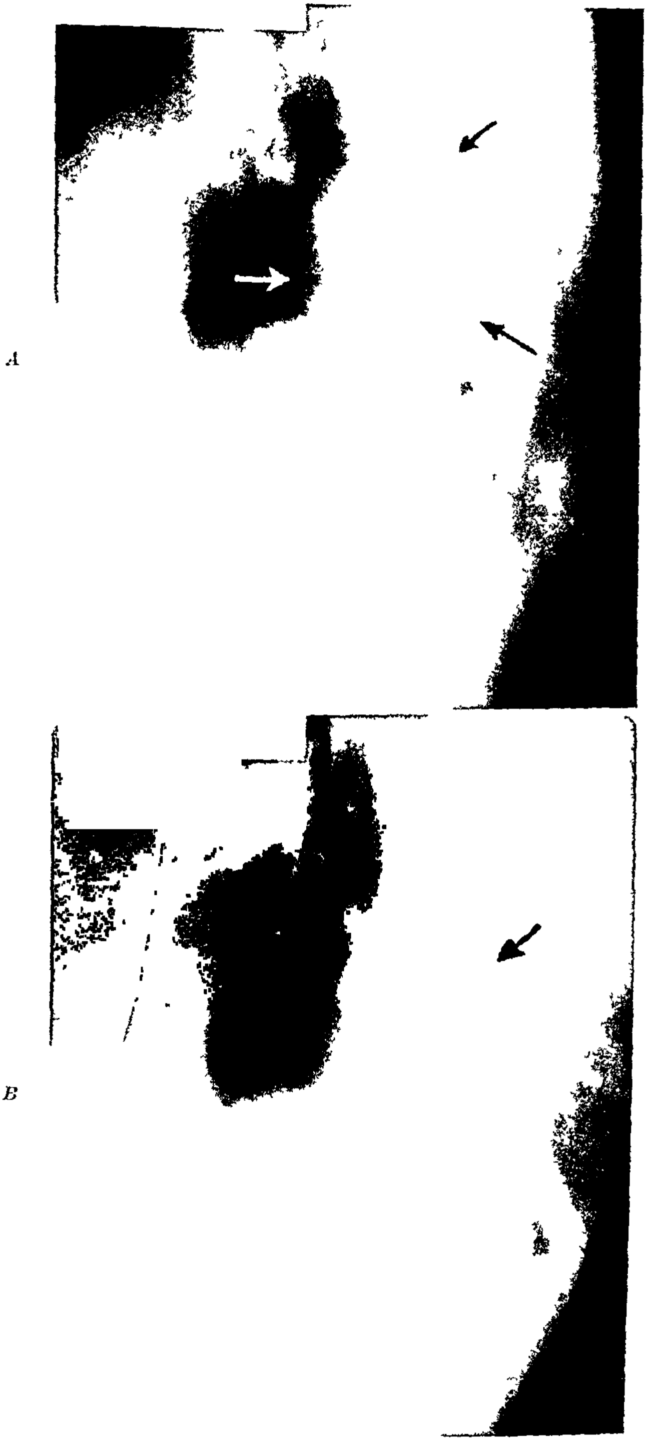


Fig 3—Lateral laminagrams of chest demonstrating (*A*) the mass (*arrows*), and (*B*) the hemivertebra (*arrow*) at the level of the origin of the meningocele

DISCUSSION

This case appears to be unique in the literature because of the severe hemorrhage. A ruptured aneurysm was the primary diagnosis since the mass could not be separated from the descending thoracic aorta by roentgenographic studies. The threat of another possibly fatal hemorrhage was one of the main reasons for exploration. The correct diagnosis was not made prior to surgery.

Although the vessels about the meningocele had undoubtedly been made more friable by the compressing hematoma which surrounded them, they had the thin-walled characteristics of vessels surrounding meningoceles in other locations.

The cause of the sudden hemorrhage could be explained by a sudden increase in intraspinal pressure and consequent expansion of the meningocele during sneezing or coughing, resulting in the rupture of one of these friable vessels. One of the patients in the cases reported by Byron, Alling and Samson[1] died of cardiac arrest following massive hemorrhage at surgery, confirming the potential danger of hemorrhage from the vessels around these lesions.

Nanson[11] reviewed the literature on intrathoracic meningocele, analyzing the published cases according to age, sex, type of lesion and whether or not there was concomitant Von Recklinghausen's disease. Cases without neurofibromatosis and kyphoscoliosis are uncommon as shown by Sears, Clayton and Siebel.[24]

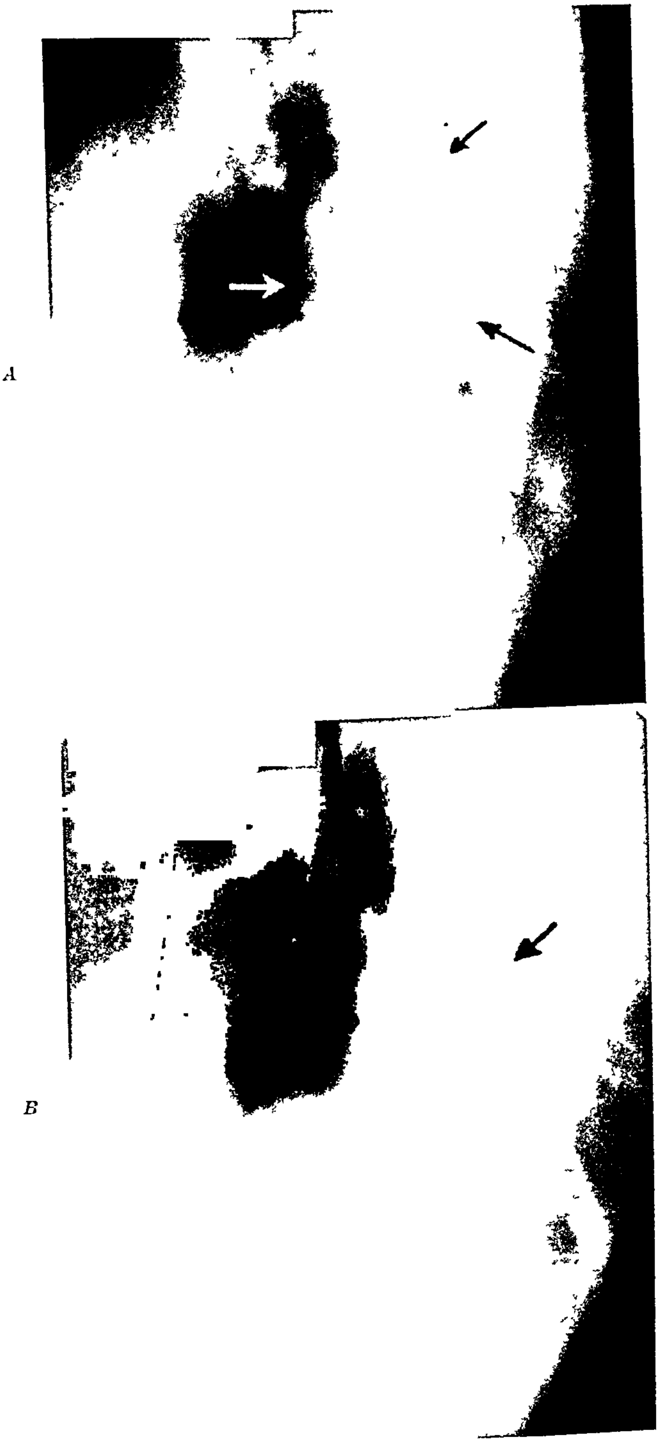
Among the 27 cases collected by Nanson there were 3 cases[6, 12, 13] in which treatment and results of treatment were unknown. Six patients were not treated,[7, 9, 13, 15, 17] with one death and unknown results in 5. One patient,[18] a 7-week old infant, had progressive respiratory distress because of the size of the tumor and died before treatment could be started. There are an additional 7 patients treated with procedures other than excision.[2, 4, 10, 19, 20, 23] Eleven patients were treated by excision.[1, 2, 4, 6, 7, 8, 11, 14, 21, 22]

The results were as follows: in the 7 patients whose treatment was other than excision there were 4 deaths, 2 living, and unknown outcome in one. Among the 11 patients treated by excision there were two surgical deaths as a result of a complicating empyema. Ours brings the total to 12 cases treated by excision, 10 successfully so. We realize that the total series of cases is small, but it seems obvious that excisional therapy yields the best results.

SUMMARY

An unusual case of the rather rare triad, von Recklinghausen's disease, kyphoscoliosis, and intrathoracic meningocele, is presented. This case distinguishes itself from other reported cases of intrathoracic meningocele by the development of a sudden massive hemothorax. The possible differential diagnosis and the therapy are presented.

A summary has been made of all previously reported cases of intrathoracic meningocele as to therapy and results. Although the total series is small, it



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MEDIASTINAL CYST WITH ESOPHAGEAL COMMUNICATION

George A. Higgins, M.D., Kansas City, Mo.*

MEDIASTINAL CYSTS constitute a significant number of the lesions of the mediastinum which are correctable by surgical excision.[2, 8, 10] Most of these cysts are of congenital origin, although there is considerable difference of opinion concerning their pathogenesis as evidenced by the variety of labels which have been attached to these interesting lesions: ciliated epithelial cysts, reduplication cysts, esophageal cysts, foregut cysts and, most commonly, bronchogenic cysts. Recently, attention has been redirected to the embryologic development of the lower respiratory tract in an effort to explain the appearance of aberrant bronchopulmonary tissue in various locations and especially to explain the appearance of aberrant pulmonary tissue having a systemic blood supply, the so-called intralobar sequestration.[4, 7] Embryologically, the lower respiratory tract first becomes apparent at an ovulation age of approximately 24 days at which time a thickening develops in the ventral wall of the foregut. This thickening rapidly develops into a bulge which then divides into right and left lung buds, and the respiratory portion of the foregut is separated from the esophageal portion by lateral ingrowths of the surrounding mesoderm to form a tracheoesophageal septum.[3] During this process of development, nests of cells may be sequestrated from either the foregut or the primitive respiratory tract and develop subsequently into isolated cysts. Some of these are carried into the substance of the pulmonary tissue and appear as bronchogenic cysts of the lung. Others retain close association with the esophagus proper, and yet others remain as isolated cysts of the mediastinum.[1, 6] To some degree, these cysts may be regarded as congenital tracheoesophageal fistulas which have become detached from the trachea and esophagus and have become closed off at each end.

Although there is general acceptance of the above explanation of the embryologic origin of cysts occurring in the substance of the lung or in close association with the lung or bronchial tree, there is some suggestion that cysts in close association with the esophagus may originate directly from the embryonic esophagus. Since the esophagus is lined by ciliated columnar epithelium at one phase of development, the presence of such lining in the adult cyst does not rule out such a mode of origin.[9] Many of these cysts have a wall consisting of two layers of smooth muscle and are devoid of cartilage, suggesting further the possibility of reduplication from the esophagus.

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*Chief Surgical Service, Veterans Administration Hospital, Kansas City, Mo.

Since both esophagus and trachea develop from a common anlage, the embryonic foregut, it seems probable that both esophageal and bronchogenic cysts may result from the separation of nests of cells during the division of the foregut into esophagus and tracheobronchial tree. There is, therefore, some basis for retaining the term "foregut cyst" since it describes both the adult morphology and the embryonic origin of these lesions.

Characteristically, the lining membrane of these cysts consists of pseudostratified columnar ciliated cells although squamous epithelium may be present, particularly in cysts closely associated with the esophagus. The wall is usually made up of smooth muscle, and cartilage is often present. The lumen is filled with a grayish-white, thick, mucoid material. When these cysts are closely associated with the tracheobronchial tree, a communication with the trachea or bronchus may occur, although this is rare. Even when closely associated with the esophagus, however, these cysts are said never to communicate directly with the lumen of the esophagus.[5] The following case is considered to be of interest for three reasons: first, there was a well-defined communication between the lumen of the esophagus and the cyst so that the cyst appeared grossly as a large diverticulum of the mid-esophagus; second, the epithelial lining of the cyst was composed alternately of stratified squamous epithelium and pseudostratified ciliated columnar epithelium; and third, this patient is of interest because of his age at the time of removal of the cyst.

CASE REPORT

W. J., a 64-year-old Negro man, entered the Kansas City Veterans Administration Hospital on Aug. 19, 1954, because of pain in the right lower costal region. There was also a history of a 20-pound weight loss during the preceding year, and the patient stated that he was having difficulty in swallowing. Except for evidence of a moderate weight loss, physical findings were noncontributory. Laboratory findings were within normal range except for a moderate hypochromic anemia and a slight elevation of serum amylase. From available records it was learned that a large cystic mass had been present in the posterior mid-mediastinum as long ago as 1935. The patient had been seen at various Veterans Administration Hospitals since that time because of other complaints; however, the mediastinal mass had apparently not interfered with his well being. Roentgenograms in various projections showed a cystic mass, measuring 14 by 10 cm., in the mid-mediastinum. There was a definite fluid level, and communication with the esophagus was present as evidenced by barium in the cyst following barium swallow (Fig. 1). The cystic structure lay mostly to the right of the midline and there was deviation of the esophagus posteriorly and to the left. Esophagoscopy showed deviation of the esophagus to the left and, 31 cm. from the upper teeth, the lumen of the cyst on the right wall of the esophagus could be seen. This lumen was of sufficient size to pass the esophagoscope into the cyst for aspiration of a large amount of undigested putrified food. Because of the evidence of superimposed infection, as well as the progressive weight loss and anemia, operative removal of the cyst was recommended.

Operation was carried out on Sept. 14, 1954. A standard right posterolateral thoracotomy was used, entering the pleural space through the bed of the sixth rib. The pleural space was relatively free of adhesions. By retracting the right lung forward, the cyst could be seen as it protruded into the right pleural space behind the hilum of the lung. The mediastinal pleura overlying the cyst was incised and the cyst was found to lie immediately below the carina, between the right and left main stem bronchi and slightly posterior Considerable difficulty was encountered in dissecting the cyst from the surrounding mediastinal structures particularly the right pulmonary veins When the cyst had been completely dissected from the surrounding structures, the wall was opened and a connection approximately 1 25 cm in diameter was found between the cyst lumen and the esophagus (Fig 2) The neck of the cyst was amputated and the resultant

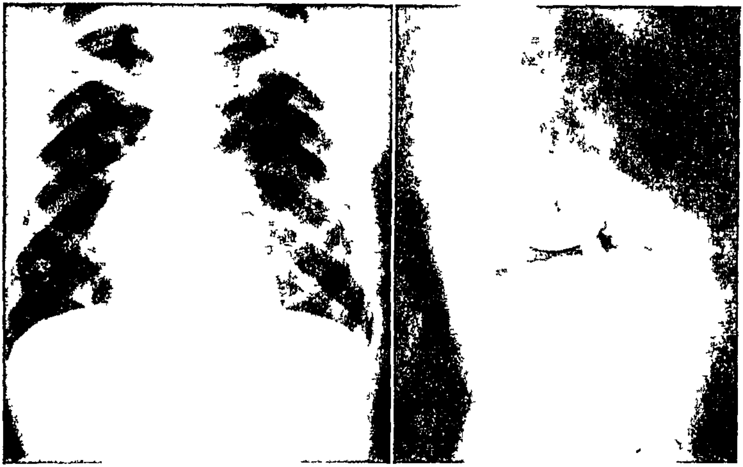

Fig 1—Roentgenograms showing cystic mass with fluid level in mid mediastinum Distortion of the esophagus and barium in the cyst are demonstrated in the lateral view

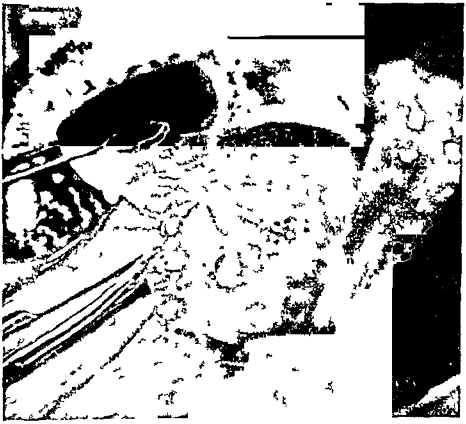

Fig 2—Photograph taken at operation showing the dissected cyst and stalk which communicated with the esophagus

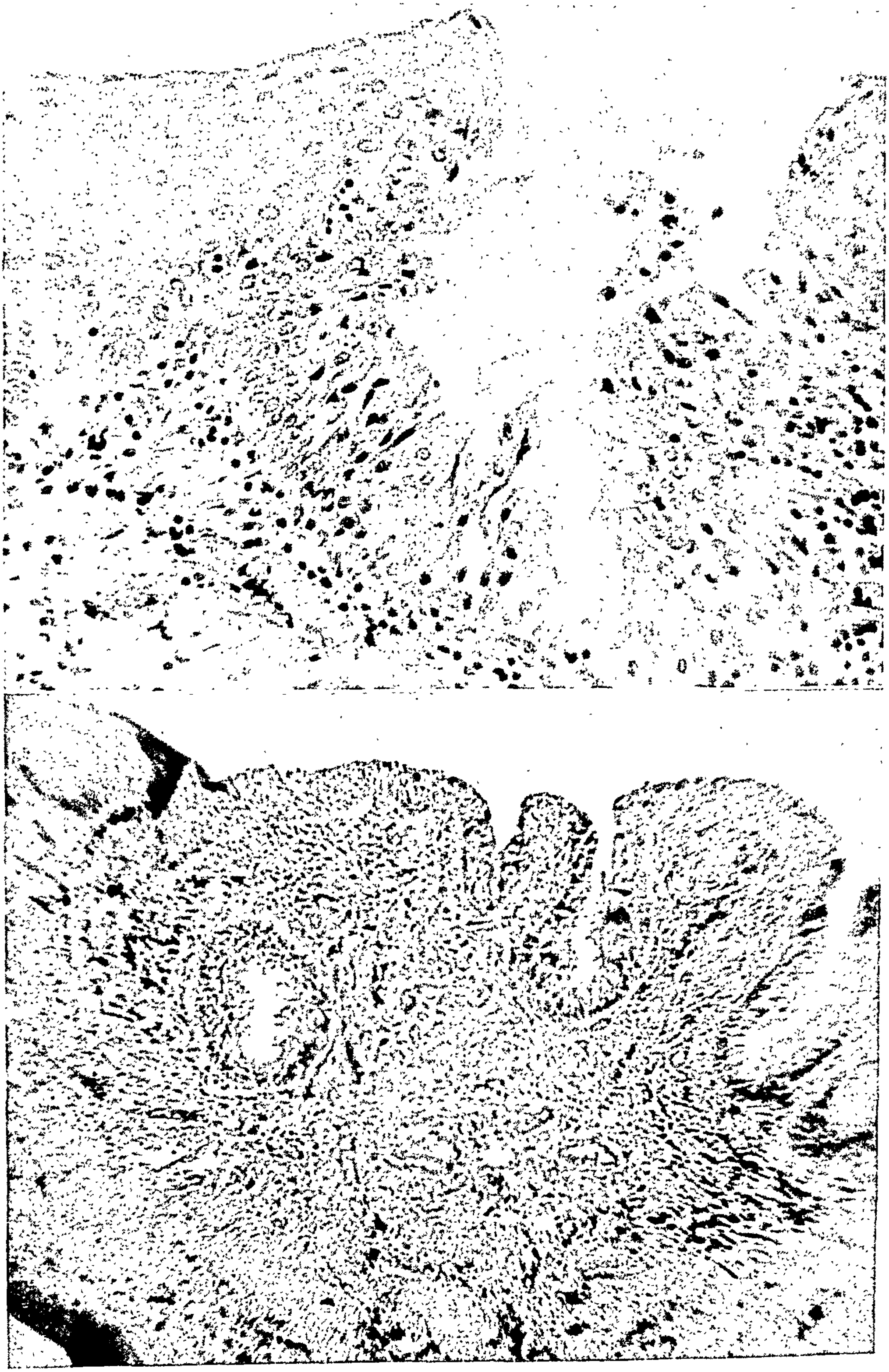

Fig. 3.—Photomicrographs of cyst lining showing both stratified squamous *epithelium* and pseudostratified ciliated columnar epithelium.

opening in the esophagus closed with interrupted sutures of fine silk, so tied that the knots were on the inside of the lumen of the esophagus A second layer of mattress stitches through the esophageal muscularis was placed for reinforcement The pleural space was flushed with saline and a tube placed in the eighth interspace for water seal drainage The chest wall was closed in layers The postoperative course was uneventful and the patient was dismissed from the hospital 4 weeks following the date of operation He has had no difficulties since operation and was last seen Nov 27, 1957, for a follow up study

The specimen consisted of a cystic structure measuring 15 cm in diameter The cyst wall was composed of a pink gray, hemorrhagic glistening smooth epithelium with one area of ulceration, approximately 1 cm in greatest diameter Microscopically (Fig 3), the epithelial lining of the cyst in part consisted of a thickened acanthotic stratified squamous epithelium showing little keratinization and morphologically similar to that ordinarily lining the esophagus In other areas, however, the epithelium was papillary and consisted of tall columnar ciliated respiratory type epithelial cells In areas there were numerous mucous type glands the ducts of which were lined with tall columnar ciliated cells The cyst wall was composed of dense collagenous fibrous tissue, with occasional small straphile bundles of smooth muscle Prolonged search of many sections failed to disclose the presence of cartilage There were no gastric or intestinal type glands present

SUMMARY

The case of a 64 year old Negro man, having a large cyst of the mid mediastinum with direct communication with the mid esophagus, is presented The epithelial lining of the cyst consisted alternately of squamous epithelium and pseudostratified ciliated columnar epithelium of the respiratory type The unusual feature of this case is the communication between the esophagus and the cyst Such a communication might possibly have resulted from spontaneous drainage of the cyst into the esophagus rather than from an embryologic communication A survey of the literature fails to reveal other instances of such a communication between the esophagus and a mediastinal cyst of this type

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ADENOCARCINOMA OF THE MIDDLE THIRD OF THE ESOPHAGUS ARISING FROM ECTOPIC GASTRIC MUCOSA

Raul A. Armstrong, M.D., John B. Blalock, M.D., and*
G. M. Carrera, M.D., New Orleans, La.

Adenocarcinoma of the esophagus is rare, being encountered less often than the epidermoid or squamous-cell type. It usually involves the lower third of the organ, where it is not always possible to differentiate the lesion from a primary tumor of the stomach. Adenocarcinoma of the middle or upper third of the esophagus is even rarer. The following case of adenocarcinoma of the middle third of the esophagus, originating from mucosa of the gastric type that completely lined the esophagus, is presented because of its rarity.

CASE REPORT

A white man, 55 years old, came to the Ochsner Clinic on Dec. 5, 1957, because of difficulty in swallowing. The only abnormality on complete physical check-up at this institution in 1953 was asymptomatic gallstones, which were demonstrated roentgenographically. Three months before admission, the patient began to experience difficulty in swallowing solid foods. This became progressively worse until, on admission, he could swallow only liquids. He had lost 8 pounds since the onset of this illness. He had not suffered from coughing, vomiting, or regurgitation of undigested food.

The only significant physical finding was poor expansion of the chest secondary to early rheumatoid spondylitis. Masses could not be palpated in the neck or abdomen. On roentgenologic examination of the gastrointestinal tract (Fig. 1, *A*), a constricting lesion of the midesophagus and an associated esophageal hiatal hernia with about two inches of stomach above the diaphragm were demonstrated. In view of these findings, the patient was hospitalized for further studies.

On esophagoscopy a constricting lesion was seen 28 cm. from the upper incisors; it was nodular, pale, friable tissue that bled easily. The tissue taken at this level by biopsy was reported as adenocarcinoma. No obvious metastatic lesions were found on thorough evaluation of the patient for operation.

On Dec. 19, 1957, esophagectomy was done through a right anterior lateral incision at the level of the third intercostal space and an upper abdominal midline incision. The tumor was found at the middle third of the esophagus at the level of the bifurcation of the trachea. The esophagus was excised from a point about 5 cm. above the tumor down through the cardia of the stomach. After a Heineke-Mikulicz type of pyloroplasty was performed, the stomach was delivered through the enlarged hiatus and esophagogastrostomy was performed at the level of the apex of the right pleural cavity.

From the Departments of Surgery and Pathology, Ochsner Clinic, New Orleans, La.
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*Fellow in General Surgery, Alton Ochsner Medical Foundation, New Orleans, La.

The postoperative course was complicated by minor separation of the cutaneous edges at the upper portion of the abdominal wound on the tenth postoperative day, and subsequent infection after secondary closure, which subsided after drainage and local application of bacitracin. Jaundice developed on the thirtieth postoperative day. This was diagnosed as homologous serum hepatitis which responded satisfactorily to therapy. Otherwise, the patient did well, tolerating feedings after the sixth postoperative day. Roentgenologic examination of the gastrointestinal tract on the eleventh postoperative day showed satisfactory anastomosis with prompt emptying of the stomach (Fig. 1, *B*). On discharge from the hospital the patient was on a regular diet, eating three meals a day.

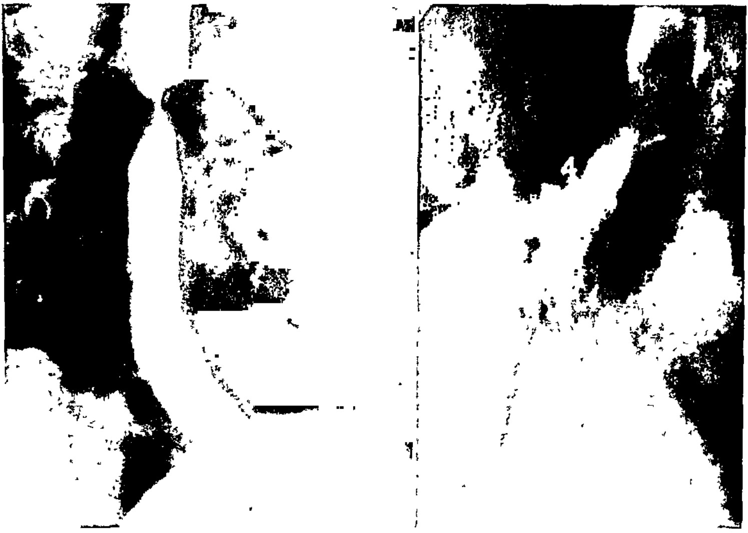
A. *B.*

Fig. 1.—*A*, Preoperative roentgenogram of the esophagus reveals a constricting lesion of the midesophagus with pronounced decrease in the size of the lumen.

B, Postoperative roentgenogram reveals the esophagogastrostomy located near the level of the sternoclavicular joint. There is an adequate lumen with prompt passage of the barium into the stomach.

The excised specimen consisted of a portion of esophagus measuring 15 cm. in length in the fixed state. Approximately 1.5 cm. from the proximal end there was an ulcerated lesion that extended for 3.5 cm. in longitudinal direction and completely encircled the esophagus (Fig. 2, *A*). It had irregular shallow borders. On section (Fig. 2, *B*), there was granular, firm, *whitish tissue which appeared to penetrate the mucosa and superficial* portion of the muscularis, but which grossly did not appear to penetrate throughout the adventitial tissues.

Microscopically, the lesion was malignant (Fig. 3). It was composed of atypical glandular structures lined by cuboidal cells with hyperchromatic nuclei and moderately abundant cytoplasm. In many areas, the glandular structures were extremely small and surrounded *by abundant fibrous stroma.* In other areas, they were slightly larger and actively invading the superficial portions of the muscular coat. In none of the sections did the tumor extend throughout the adventitia. The remainder of the specimen contained glandular mucosa of gastric type with no parietal cells. There was no evidence of the normal esophageal stratified squamous epithelium (*Fig. 3*). There was no evidence of metastasis in the regional lymph nodes.

DISCUSSION

Incidence.—The first case of adenocarcinoma of the esophagus was reported by White in 1898, according to Carrie.[1] In a review of the medical literature in 1900, Hewlett[2] was able to find only 6 cases, all of which were located in the lower third. More recently, Smithers[3] reported 26 cases of adenocarcinoma among 314 primary tumors of the esophagus seen at the Royal Marsden Hospital between 1936 and 1951, an incidence of 8 per cent. Puestow, Gillesby and Guynn,[4] in 1955, reported a 10 per cent incidence of adenocarcinoma among 603 cases of carcinoma of the esophagus encountered during a period of 23 years at the Veterans Administration Hospital in Hines, Ill.

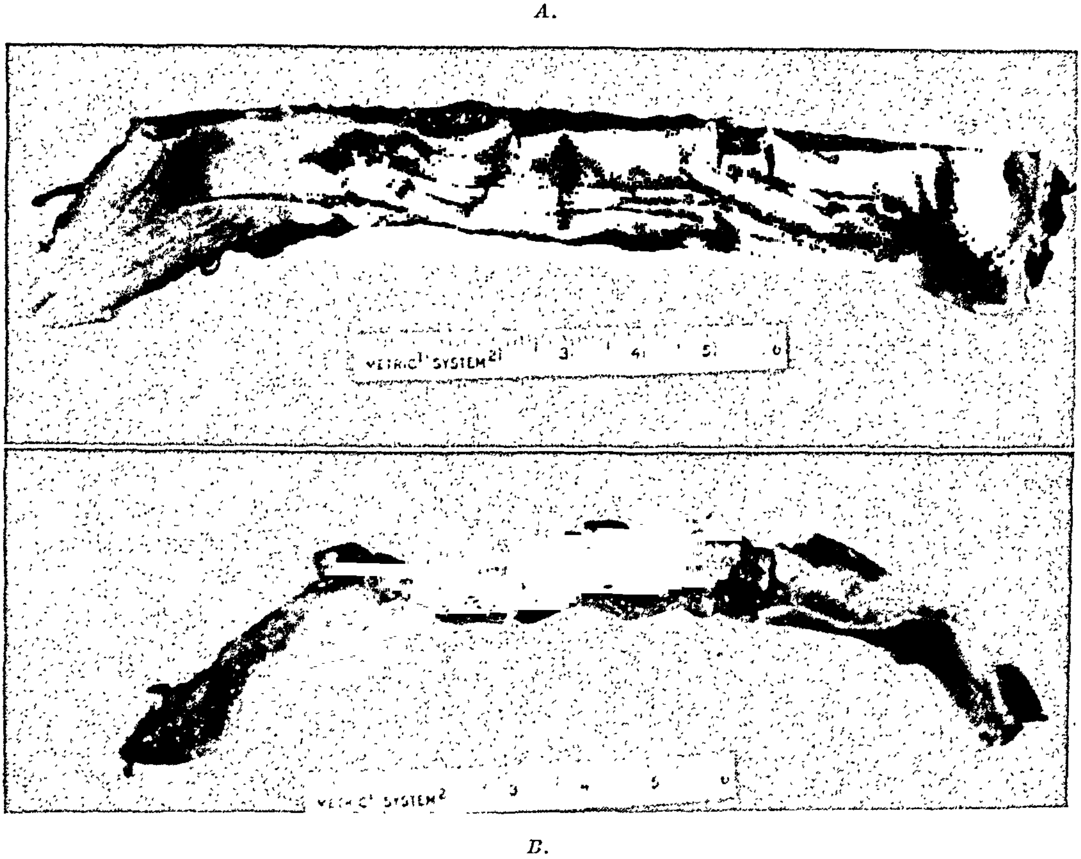

Fig. 2.—*A*, Photograph of open specimen, after fixation, which reveals the tumor near the upper border of the specimen (left side of the illustration).
B, Photograph of side view which reveals the tumor extending through the entire thickness of the wall but not involving the adventitia.

The earlier reports included adenocarcinoma of only the lower third of the organ. The more recent reports, however, include adenocarcinomas in the middle and upper thirds. In 1939, Feldman[7] reported a case of an adenocarcinomatous polyp of the upper part of the esophagus and, in 1949, Carrie[1] reported what appears to be the first case of an adenocarcinoma of the upper end of the esophagus arising from a patch of ectopic gastric epithelium. He reviewed 19 other cases of esophageal adenocarcinoma seen in his department

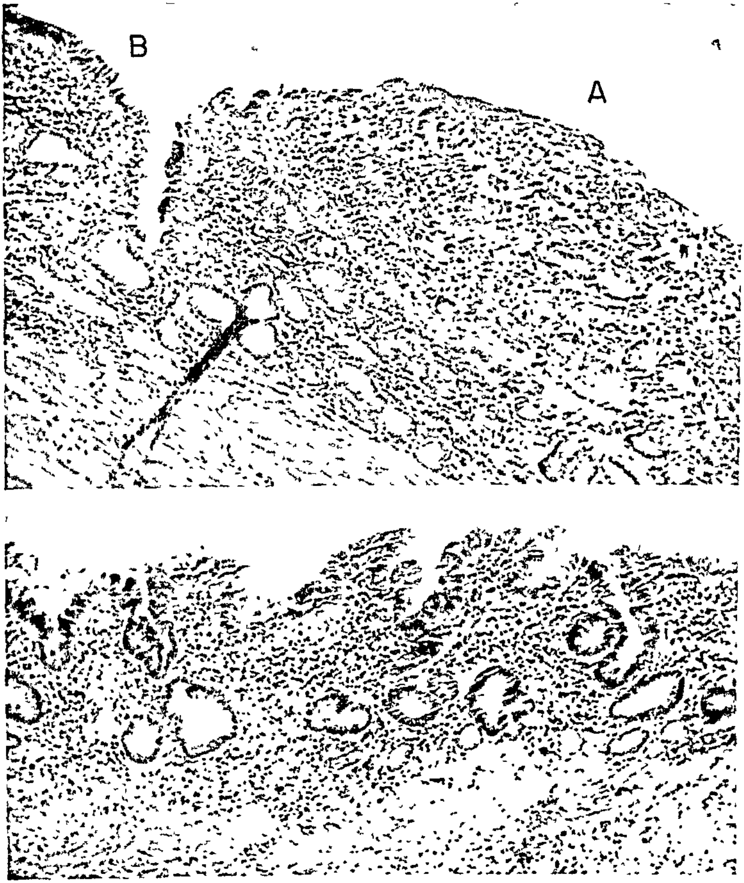

Fig 3.—*Upper,* Photomicrograph of section through the upper border of the tumor reveals *(A)* a malignant neoplasm composed of atypical glandular structures lined by cuboidal cells with hyperchromatic nuclei. *B,* Mucosa of gastric type is seen at the border of the tumor.

Lower, Photomicrograph of section through the wall of the esophagus at some distance from the tumor reveals mucosa of gastric type. No squamous-cell type of epithelium is seen lining the esophagus.

during a period of 15 years, all of which were in the lower end. In 1956, Smithers[3] described one case of adenocarcinoma in the upper third and 3 cases in the middle third of the esophagus, among 23 cases of adenocarcinoma that were studied. In the report of Puestow and associates[4] were 5 cases of adenocarcinoma arising in the esophagus at some distance from the cardia.

More recently, McCorkle and Blades[6] reported a case of adenocarcinoma arising in the middle third of the esophagus which was treated by esophagectomy and esophagogastrostomy. The patient subsequently died and, at postmortem examination, the esophageal mucosa was completely replaced by mucosa of the gastric type from the cardia up to a few centimeters below the pharynx.

Origin.—The origin of adenocarcinoma of the esophagus has been studied by various authors. Smithers[3] postulated that there are three possible origins of true adenocarcinomas of the esophagus (as distinguished from primarily gastric tumors): (1) ectopic islets of gastric mucosa, or esophageal glands, (2) esophageal mucous membrane that failed to undergo squamous transformation before birth, and (3) mucosa that underwent glandular metaplasia after chronic infection. This classification includes, totally or in part, most of the theories advanced to explain the presence of glandular epithelium that could eventually give rise to an adenocarcinoma in an organ normally lined by stratified squamous epithelium.

The presence of aberrant (ectopic) gastric mucosa was first described by Schmidt in 1805, according to McCorkle and Blades.[6] The incidence is not established and varies widely according to existing reports. Schridde[7] found aberrant islets of gastric mucosa in the postericoid region in 70 per cent of necropsies. Carrie[1] described islands of ectopic gastric mucosa on the lateral walls of the esophagus between the level of the cricoid cartilage and the fifth tracheal ring in about 50 per cent of the patients examined. Rector and Connerley[8] found some form of gastric mucosa in the esophagus in 78 of 1,000 consecutive necropsies performed on infants and children, or an incidence of only 7.8 per cent. These ectopic islands were found to be more common in the upper (51 per cent) and middle thirds (41 per cent) than in the lower third (8 per cent).

The presence of esophageal glands was verified by Carrie,[1] who actually described two types of glands, a submucosal mucous-secreting gland, and some superficial ones resembling gastric glands occurring at both ends of the esophagus. This last group corresponds to the ectopic islets of gastric mucosa described by other authors.

The theory by which an originally squamous type epithelium undergoes glandular metaplasia after a chronic infection, and then undergoes carcinomatous degeneration, has also been advanced, but we were unable to find any cases in which this sequence could definitely be established.

Barrett[9] recently suggested that when the lower part of the esophagus is lined by columnar epithelium, which corresponds to Smithers' second postulate, the condition is due to failure of the embryonic lining of the gullet to achieve maturity The case reported by McCorkle and Blades[6] and our case are examples of this condition, in which the entire organ failed to undergo squamous transformation

SUMMARY

A case of adenocarcinoma of the middle third of the esophagus, arising from mucosa of gastric type that completely relined the esophagus, has been presented Adenocarcinoma of the esophagus is a true entity that can originate from ectopic patches of gastric mucosa, from esophageal glands, or from esophageal mucous membrane that failed to undergo squamous transformation before birth

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PERICARDITIS WITH MASSIVE CASEATION

Jacob K. Berman, M.D., Victor Mori, M.D., and Anthony Ridolfo, M.D., Indianapolis, Ind.

THE PURPOSE of this paper is to record a case of tuberculous pericarditis with massive caseation associated with active miliary pulmonary tuberculosis. The patient was successfully treated by pericardiectomy.

Tuberculous pericarditis in its various stages has been exhaustively studied and described, and the existence of pericardial caseation is mentioned by many authorities.[3-8] Holman[5] was one of the first to advocate pericardiectomy in active tuberculous pericarditis. He reported 4 cases, and then added a fifth, of successful pericardiectomy in the active phase of the disease. All of his patients had positive cultures and 1 showed caseating tuberculous granulation tissue. In a later paper,[6] he reported 8 patients with proved tuberculous pericarditis who survived pericardiectomy. Six of these had active pulmonary tuberculosis. Our experience supports his conclusions that pericardiectomy done during the early periods can be accomplished with greater ease than is possible in the advanced stage. Also, early pericardiectomy may prevent myocardial involvement seen so commonly in far-advanced constrictive pericarditis, and may also prevent the secondary effects of increased venous pressure.

CASE REPORT

M. M., a 30-year-old Negro woman, came to the Indianapolis General Hospital on May 30, 1957, because of persistent substernal pain, dyspnea, chills, and fever. There had been no menstruation for the previous 2 months and the patient ascribed her thirst, frequent urination, and nocturia to the amenorrhea.

The patient had been seen in the medical clinic at frequent intervals because of a persistent cough. X-ray studies of the chest dating back to 1944 were reviewed, and no definite abnormalities were noted. A film taken 1 year before the present illness was normal (Fig. 1, *A*).

The patient was orthopneic; however, there was no distention of the neck veins and no facial edema. Her temperature was 101.2° F., the blood pressure was 106/60 mm. Hg and the pulse was 80 and regular. The point of maximum impulse was slightly displaced to the left and cardiac dullness was increased, but we were unable to detect any murmurs and the breath sounds were clear. There was no evidence of ascites and the liver was normal in size. Bimanual examination showed the uterus to be slightly enlarged and symmetrical, with a soft lower uterine segment.

From the Department of Surgery and the Robert M. Moore Heart Clinic, Indianapolis General Hospital, Indianapolis, Ind.

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The more important laboratory findings were as follows: The hemoglobin was 8 Gm.; erythrocytes numbered 2.8 million; and leukocytes 5,850. The urinalyses were normal except for 2+ pus on one occasion. Tuberculin purified protein derivative test, first strength, was negative, but second strength was strongly positive. The frog test for pregnancy was positive. The electrocardiogram showed nonspecific T-wave changes (Fig. 2). X-ray showed enlargement of the cardiac shadow (Fig. 1, *B*). We thought that the patient had tuberculosis and tuberculous pericarditis with effusion. She was in the first trimester of pregnancy, and we believed that this may have been an important factor in the present acute exacerbation.

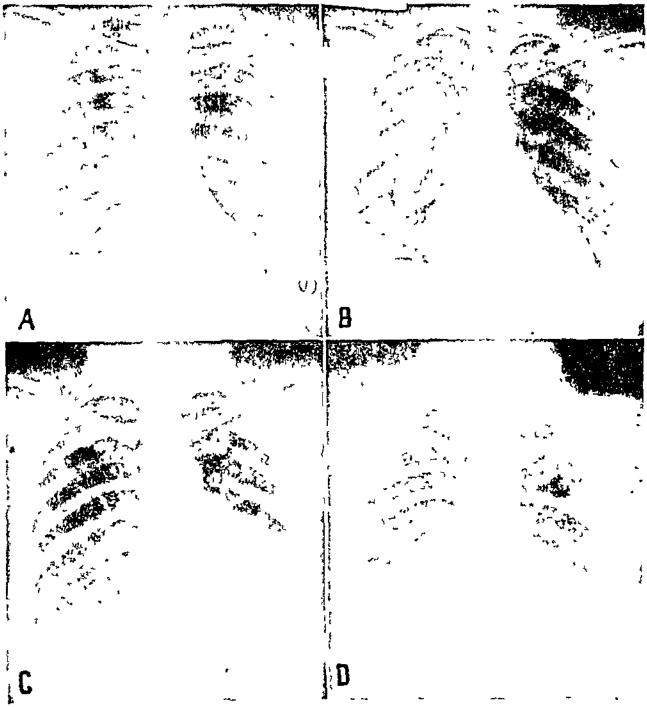

Fig 1.—*A*, X-ray taken 1 year before the present illness The transcardiac diameter is 12 cm and the transthoracic diameter is 27 cm.

B, X-ray taken on admission The transcardiac diameter is 16 cm. There are no pulmonary changes which would indicate cardiac failure or miliary tuberculosis

C, X-ray taken 41 days after admission. The cardiac silhouette extends to the thoracic wall

D, X-ray taken 6 months after pericardiectomy.

During the first 2 weeks in the hospital the remittent fever ranged up to 103° F. She was given various types of antibiotics, including penicillin, streptomycin, Achromycin, Albamycin, and also chemotherapeutic agents, such as gantrisin, for an associated cystitis. The fever gradually decreased, then became intermittent, varying between normal and 100° F. Eight weeks after admission the temperature became normal and remained so.

The pulse was 80 on admission, but soon reached 120 and remained at this rate until 6 days after admission. At this time the blood culture showed *Staphylococcus aureus* which was coagulase positive. It was found to be resistant to all antibiotics except Albamycin. Cultures from the sputum, gastric juice, urine, and bone marrow were negative for acid-fast bacilli.

We could now hear a pericardial friction rub. Pericardiocentesis yielded 40 c.c. of slightly cloudy, yellowish-green fluid. No acid-fast organisms were found on direct smear and none were cultured from this exudate. On the forty-first hospital day, cardiac fluoroscopy showed the left ventricle to be greatly enlarged and heart pulsations diminished. The friction rub could no longer be heard, and the pulse rate was 130. The venous pressure in the right antecubital vein was 20 cm. of water.

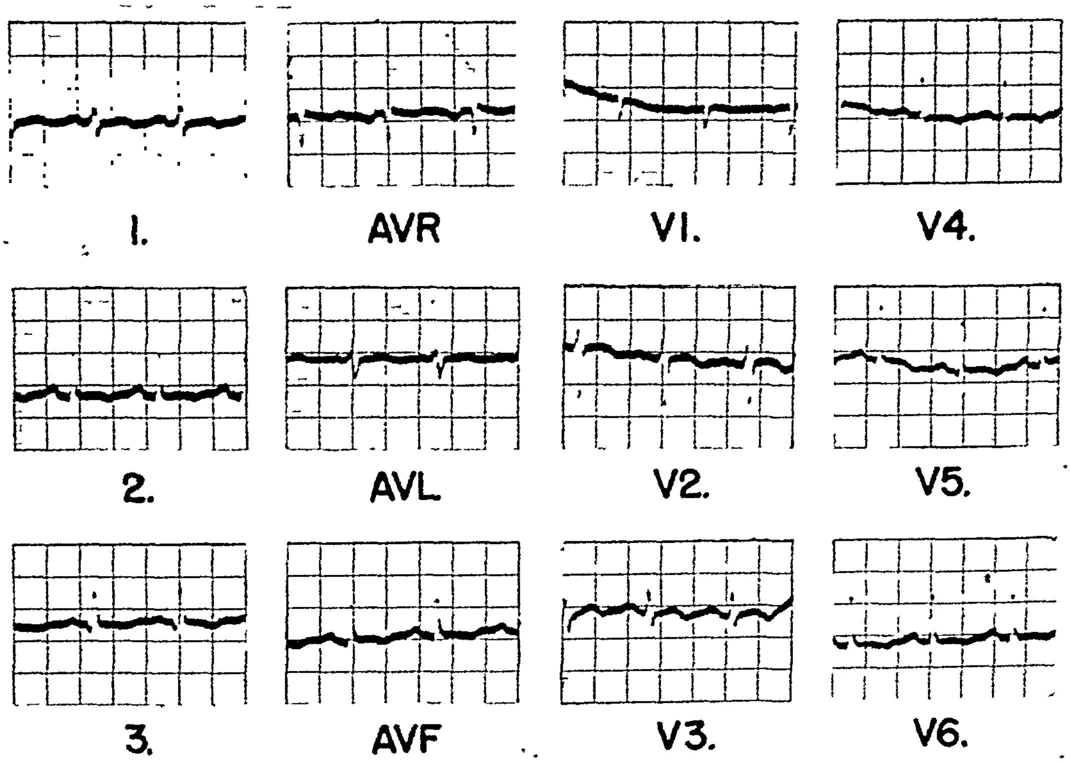

Fig. 2.—Electrocardiogram taken preoperatively, which shows inverted T waves in Leads II, III, aVF, V_2, V_3, V_4, V_5, and V_6.

Left thoracotomy was done on the fifty-seventh hospital day. The lung was found to be densely adherent to the pericardium and several pockets of localized effusion were encountered between the lung and the fibrous pericardium. Heart motion was barely perceptible under the thickened and shaggy pericardium. The fibrous pericardium was peeled carefully from over the left ventricle. It was roughly 1.5 cm. thick. The phrenic nerve was dissected out and retracted laterally. As the serous pericardium was being peeled off, a large abscess cavity was encountered. It was filled with thick, gray-white caseous material and measured about 8 by 10 cm. The entire cavity was unroofed, and the left ventricle and the left atrium were found to be covered with caseous material which could be removed easily (Fig. 3). The pericardium over the right ventricle varied in thickness between 1 to 1.5 cm., and therefore a pericardiectomy was done, including the removal of a thickened fibrous extension over the superior and inferior venae cavae. The epicardium over the right heart oozed considerably. The lung was studded with miliary tubercles involving all lobes. A small portion of the lingula was removed for microscopic study and for culture.

No organisms were found on direct smear from the pericardium and none grew in culture. Studies of the pericardium showed changes characteristic of tuberculosis. Biopsy of the lung also showed typical tuberculous granulation tissue.

Postoperatively, the patient was given 0.5 Gm. streptomycin twice daily and 300 mg. isonicotinic acid hydrazide daily. Her recovery was uncomplicated and she was released from the hospital 3 weeks after surgery.

The pregnancy progressed without complications and 6 months after surgery the patient delivered a healthy female infant, weighing 6 pounds 10 ounces. The placenta showed no evidence of tuberculosis. X-rays made at this time showed great improvement (Fig. 1, *D*). Tubal ligations were deemed advisable by the obstetrical department, and were done 4 days after delivery. No evidence of tuberculosis was apparent in the abdominal cavity except on the anterior surface of the liver, here one hard calcified nodule was described. A biopsy was not taken. There were no postoperative complications or sequelae. Tuberculin skin tests made on the infant at 4 months were negative.

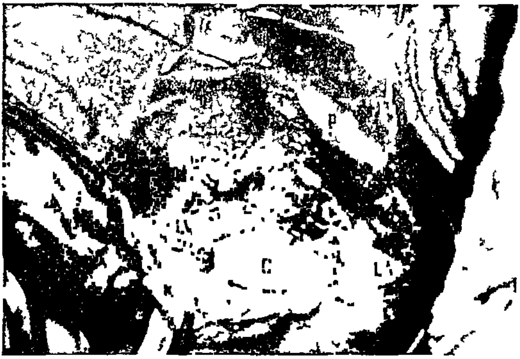

Fig. 3.—Photograph taken at the time of surgery. *C*—area of caseation. *LA*—left atrium. *LV*—left ventricle. *P*—thickened pericardium.

DISCUSSION

The blood culture on one occasion showed *Staphylococcus aureus* which was coagulase positive. No other blood or tissue cultures produced a growth of this organism. Yet the abruptness of onset and the characteristic chills and fever must be regarded as more typical of the so-called suppurative, or nonspecific, infections than of tuberculosis. However, it is well to recall that the old "florida phthisis" type of tuberculosis was indeed a tuberculous septicemia so acute and virulent that the antigen evoked a response not unlike that of staphylococcic septicemia. Conversely, in the chronic staphylococcic infection of bone clinically described as Brodie's abscess, the staphylococcus is weak and its numbers are few and the tissue response is "cold" as in tuberculosis.[7] The single preoperative blood culture of *Staphylococcus aureus* in our case must be regarded either as a contamination or a transient infection which was readily controlled by antibiotics.

The histopathologic changes in the surgical specimens were those of a granulomatous lesion characteristic of tuberculosis. However, no microorganisms of any sort were found. The explanation [illegible] nce of tubercle bacilli is debatable. However, it is well known that when the capsule of the tubercle bacillus is fractionated, phospholipids are obtained that have the property of stimulating a reaction similar to tuberculosis due to the presence of phthioic acid.[1] This is particularly true in sensitized rabbits. Perhaps, in caseating lesions, necrosis of the tubercle bacillus occurs with cellular destruction and the antigenic factor may be phthioic acid.

Tuberculous pericarditis in our experience begins with some minimal pericardial effusion (moist form) or as a fibrocaseous lesion (dry form), or by effusion in some areas and coagulation necrosis in others, simultaneously. We have never encountered widespread caseation. The ultimate result is fibrosis and calcification, first over the right ventricle at its lower border and then over the left ventricle.[6]

The effectiveness of antibiotics and chemotherapeutic agents in miliary tuberculosis, and pericardiectomy in early tuberculous constrictive pericarditis, is dramatically demonstrated by this case. The miliary tuberculosis appeared to be foreboding. However, the patient's recovery has been comparatively rapid and complete.

SUMMARY

This is a case report of a patient with diffuse miliary pulmonary tuberculosis appearing in the early trimester of pregnancy and associated with tuberculous pericarditis with massive caseation treated by pericardiectomy. She had a sponntaneous delivery of a healthy baby at term. The patient and her baby were last seen 10 months after pericardiectomy. Both are apparently well.

We are grateful to Dr. Charles Fisch, Director of the Robert M. Moore Heart Clinic, Dr. William Tosick, Radiologist, and Dr. Paul Evans, Pathologist of the Indianapolis General Hospital, for their kind assistance.

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THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Thirty-Ninth Annual Meeting

April 21, 22, and 23, 1959

Statler Hilton Hotel, Los Angeles, Calif.

Program

Memoranda for Guidance of Speakers

1. In accordance with the By-Laws of the Association the papers which are read at the meeting shall be given to the Reporter *immediately after presentation.* If these papers are not submitted promptly their publication may be delayed.
2. In publication it is customary to group discussions together on a series of papers. Any delay in the return of corrected discussions to the Editor means that publication of all papers on the subject will be held up. This is manifestly unfair to those who are conscientious in the prompt submission of their remarks for publication. Undue tardiness may mean that the discussion will not be published.
3. *Regular Program.* Speakers will be limited to 15 minutes.
4. *Thoracic Surgery Forum.* Speakers will be limited to 10 minutes. Papers on the Thoracic Surgery Forum as submitted for publication will be limited to 3,000 words. At the discretion of the President limited discussion will be allowed following the formal presentations.
5. *Discussion of Papers.* Discussers will be limited to 3 minutes. Only members of the Association and invited speakers will have the privilege of discussing papers.

Tuesday Morning, April 21, 1959

8:30 A.M. Business Meeting

Scientific Session. Regular Program

1. **Studies of Pulmonary Diffusion After Open Heart Surgery.** Robert F. Schramel (by invitation), Robert Cameron (by invitation), Morton Ziskind (by invitation), Maurice Adam (by invitation), and Oscar Creech, Jr., New Orleans, La.
2. **Clinical Results of Correction Under Hypothermia of Atrial Septal Defects and Pulmonary Valvular Stenosis.** Earle B. Mahoney, James A. Manning (by invitation), James A. DeWeese (by invitation), and Seymour I. Schwartz (by invitation), Rochester, N. Y.
3. **Simplified Technique for Direct Vision Pulmonary Valvotomy.** Conrad R. Lam, and Rodman E. Taber, Detroit, Mich.
4. **Surgical Treatment of Isolated Pulmonary Infundibular Stenosis.** William P. Hederman (by invitation), S. Gilbert Blount (by invitation), and Henry Swan, Denver, Colo.
5. **Surgical Experiences in the Treatment of Congenital Mitral Stenosis and Mitral Insufficiency.** George W. B. Starkey, Boston, Mass.
6. **The Etiology and Prevention of Atrial Fibrillation After Mitral Valvotomy.** C. Frederick Kittle, and James Crockett (by invitation), Kansas City, Kan.

Tuesday Afternoon, April 21, 1959

2:00 P.M. Scientific Session: REGULAR PROGRAM

7. **The Surgical Management of Complications of Staphylococcal Pneumonia in Infancy and Childhood.** David C. Sabiston, Jr., Edward W. Hopkins (by invitation), and Robert E. Cooke (by invitation), Baltimore, Md.
8. **Surgical Treatment of Pulmonary Coccidioidomycosis: Ten-Year Study.** Bert H. Cotton, and J. W. Birsner (by invitation), Pasadena, Calif.
9. **The Effect of Mean Endotracheal Pressure on the Cardiac Output of Patients Undergoing Intrathoracic Operations.** Thomas F. Nealon, Jr., Richard T. Cathcart (by invitation), William Fraimow (by invitation), Edward D. McLaughlin (by invitation), and John H. Gibbon, Jr., Philadelphia, Pa.
10. **Injuries of the Trachea and Major Bronchi.** R. Maurice Hood, Austin, Texas, and Herbert E. Sloan, Ann Arbor, Mich.
11. **Adverse Surgical Experience in the Treatment of Pulmonary Disease Caused by Atypical Acid-fast Bacilli.** Robert W. Harrison (by invitation), Arthur F. Reimann (by invitation), Edwin T. Long (by invitation), William Lester, Jr. (by invitation), and William E. Adams, Chicago, Ill.
12. **The Surgical Treatment of Tuberculosis in Children.** Walter W. Fischer, New York, N. Y.
13. **Persistent Pleural Air Space Following Resection for Pulmonary Tuberculosis.** T. W. Shields (by invitation), Wm. M. Lees, R. T. Fox, and G. Salazar (by invitation), Chicago, Ill.

Wednesday Morning, April 22, 1959

8:30 A.M. Scientific Session: THORACIC SURGERY FORUM

14. **Metabolic Acidosis and the Dissociation Curve of Hemoglobin During Extracorporeal Circulation.** George J. Magovern (by invitation), Robert S. Cartwright (by invitation), John F. Neville, Jr. (by invitation), and Edward M. Kent, Pittsburgh, Pa.
15. **Studies of a New Donor Blood Anticoagulant-Preservative Mixture for Extracorporeal Circulation.** Wirt W. Smith (by invitation), Ivan W. Brown, Jr., W. Glenn Young (by invitation), and W. C. Sealy, Durham, N. C.
16. **Simple, Automatic, Self-Regulating Heart-lung Machine Pump.** Josh Fields (by invitation), Francis X. Byron, and William C. Dale (by invitation), Beverly Hills, Calif.
17. **An Improved Inexpensive Automatically Controlled Pump-Oxygenator.** Adrian Kantrowitz (by invitation), and Donald Abelson (by invitation). Sponsored by Alfred Hurwitz, Brooklyn, N. Y.
18. **An Externally Valved Hydraulic Cardiac Substitute.** I. A. Breckler (by invitation), R. L. Ginsberg (by invitation), C. L. Portnoff (by invitation), and Jack L. Bitterly (by invitation), Encino, Calif.
19. **Physiologic P Wave Cardiac Stimulator.** Sam E. Stephenson, Jr. (by invitation), W. H. Edwards (by invitation), P. J. Jolly (by invitation), and H. W. Scott, Jr., Nashville, Tenn.
20. **"Tranquilization" of the Heart With the Ataractic Drugs.** Russell M. Nelson, Salt Lake City, Utah.
21. **The Mechanism of Ventricular Fibrillation and Cardiac Arrest During Surgery.** Archer S. Gordon (by invitation), and John C. Jones, Los Angeles, Calif.
22. **Prevention of Post-Hypercapneic Ventricular Fibrillation in Dogs.** Bernard Goott (by invitation), Fletcher A. Miller (by invitation), and Owen H. Wangensteen, Minneapolis, Minn.

23. **A Method for the Simultaneous Measurement of Maximum Breathing Capacity, Pulmonary Volumina, and Effective Lung Ventilation.** George W. Wright, and Sol Guilford (by invitation), Cleveland, Ohio.

24. **A New Foam Plastic Arterial Prosthesis.** Richard W. Hardy (by invitation), *Washington, D. C.*

25. **Experimental Observations on Poststenotic Dilatation.** David L. Bruns (by invitation), John E. Connolly (by invitation), Emile Holman, and Raymond C. Stofer (by invitation), San Francisco, Calif.

26. **Surgical Management of Metallic Foreign Bodies in the Pulmonary Artery. Experimental and Clinical Observations.** Lyman A. Brewer, III, Edward L. King (by invitation), Ellsworth F. Wareham (by invitation), and Jack M. Farris (by invitation), Los Angeles, Calif.

27. **The Cause of Death Following Cardioangiography.** Raymond C. Read (by invitation). Sponsored by Richard L. Varco, Minneapolis, Minn.

28. **Physiologic Response of the Coronary Circulation to Unilateral Pulmonary Artery Ligation.** James B. Littlefield (by invitation), Phyllis R. Ingram (by invitation), and William H. Muller, Jr., Charlottesville, Va.

Wednesday Afternoon, April 22, 1959

2:00 P.M. Executive Session (Limited to Active and Senior Members)

3:00 P.M. Scientific Session. REGULAR PROGRAM

Address by the President, Michael E. De Bakey, Houston, Texas.

29. **Surgical Treatment of Cylindroma of the Bronchus (Adenoid Cystic Carcinoma).** W. Spencer Payne (by invitation), F. Henry Ellis, Jr., Lewis B. Woolner (by invitation), and Herman J. Moersch, Rochester, Minn.

30. **Bronchogenic Carcinoma. An Aggressive Surgical Attitude.** J. Maxwell Chamberlain, Thomas M. McNeill (by invitation), John R. Edsall (by invitation), and Peter Parnassa (by invitation), New York, N. Y.

7:00 P.M. Banquet and Dancing, Statler Hilton Hotel.

Attendance limited to Members of the Association and their ladies, invited speakers and their ladies.

Dinner dress preferred.

Thursday Morning, April 23, 1959

9:00 A.M. Scientific Session. REGULAR PROGRAM

31. **Instantaneous Blood Loss Determination in Thoracic Surgery.** Robert Klopstock, Harry H. LeVeen (by invitation), and Phillip I. Levitan (by invitation), Brooklyn, N. Y.

32. **Experiences With the Treatment of Postoperative Cardiac or Respiratory Failure With a Mechanical Respirator.** J. C. Spencer, D. W. Benson (by invitation), W. C. Liu (by invitation), and H. T. Bahnson, Baltimore, Md.

33. **Intrathoracic Complications of Subdiaphragmatic Infection.** David P. Boyd, Boston, Mass.

34. **The Early Elective Surgical Approach to the Treatment of Traumatic Hemothorax.** Morris M. Culiner (by invitation), Benson B. Roe, and Orville F. Grimes, San Francisco, Calif.

35. **The Surgical Treatment of Peptic Esophagitis.** Frederick S. Cross, George A. Smith, Jr. (by invitation), and Earle B. Kay, Cleveland, Ohio.

36. **Utility of a New Procedure of Valvular Esophagogastrostomy in Cases of Brachyesophagus and Stricture. Clinical and Experimental Studies.** David H. Watkins, William R. Rundles (by invitation), and Louis Tatom (by invitation), Denver, Colo.

Thursday Afternoon, April 23, 1959

2:00 P.M. Scientific Session: REGULAR PROGRAM

37. **The Relationship of Postoperative Acidosis to Pulmonary and Cardiovascular Function.** George H. A. Clowes, Jr., Andrzej Alichniewicz (by invitation), Louis del Guercio (by invitation), and David Gillespie (by invitation), Cleveland, Ohio.
38. **Surgical Treatment of Chronic Pericarditis.** W. S. Blakemore, C. K. Kirby, H. F. Zinsser, Jr. (by invitation), W. B. Whitacre (by invitation), and J. Johnson, Philadelphia, Pa.
39. **The Results of Surgical Correction of Atrial Septal Defect Complicated by Pulmonary Hypertension.** Bert W. Meyer, John C. Jones, and Harold V. Liddle (by invitation), Los Angeles, Calif.
40. **Coarctation of the Aorta in Infants: A Clinical and Experimental Study.** Thomas B. Ferguson, Thomas H. Burford, and David Goldring (by invitation), St. Louis, Mo.
41. **Problems in the Surgical Management of Coarctation of the Aorta: Based on Experience With Sixty Consecutive Cases.** L. K. Groves and D. B. Effler, Cleveland, Ohio.
42. **An Analysis of Deaths Following Cardiac Surgery.** James L. Harrison (by invitation), Bart D. Iaia (by invitation), and Robert P. Glover, Philadelphia, Pa.

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Original Communications

SARCOMA OF ESOPHAGUS: SURGICAL TREATMENT

John Borrie, Ch.M., F.R.C.S., Dunedin, New Zealand

INTRODUCTION

Although sarcomas of the esophagus are rare, the present-day wider appreciation that dysphagia means mechanical foregut obstruction which can usually be relieved and often cured by operation ensures that patients suffering from sarcoma of the esophagus will, from time to time, present themselves for treatment. What sarcomas of the esophagus treated surgically have been reported, and what are the results of such treatment?

The purpose of this paper is briefly to review published reports of surgical treatment of this lesion, to describe one further patient who, in 1952, was found to have a polypoid fibrosarcoma in the lower third of the esophagus one year after successful hiatal herniorrhaphy, and to report his continued good health 6 years after partial esophagogastrectomy (Table I).

PATHOLOGY

The first case of sarcoma of the esophagus was reported by Chapman[1] in 1877. The pathologic types and clinical features have been fully described in the past, especially by Dvorak,[2] who reviewed reported cases up to 1931, and ably discussed these particular aspects of the subject. Thorek and Neiman,[3] in 1950, collected 58 proved cases of sarcoma of the esophagus, which included 30 fibrosarcomas, 8 leiomyosarcomas, 5 lymphosarcomas, 5 melanosarcomas, 3 rhabdomyosarcomas, and 7 unclassified sarcomas. According to Ewing,[4] the age incidence varies from 4 to 70 years. These tumors are most commonly found in the lower third of the esophagus, and may vary greatly in size.

From the Department of Surgery, University of Otago, and Thoracic Surgical Department, Dunedin and Wakari Hospitals, New Zealand.

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Ewing describes two general types of growth, namely the *polypoid* and *ulcerative* forms. The former arise from the submucosa, are slow growing, they form a polypoid mass within the lumen of the esophagus, cause little tissue destruction, and they metastasize late. The latter grow rapidly, infiltrate widely, and ulcerate, with hemorrhage, focal necrosis, and even perforation.

CLINICAL FEATURES

These may advance more rapidly than with carcinoma of the esophagus. The commonest symptom is dysphagia, and is early associated with pain, which may be nocturnal and not associated with food. Weight loss accompanies the dysphagia, and Thorek and Neiman stress that when the degree of wasting is out of proportion to the degree of dysphagia, a sarcoma should be suspected rather than carcinoma. Further, they claim that sarcoma of the esophagus is more rapidly fatal than carcinoma, the patient rarely living more than 6 months after the onset of dysphagia. Although study of the cases in which there was surgical treatment does not confirm this, nevertheless long-term survival after successful surgical removal must remain closely related to early diagnosis and early appreciation of the significance of symptoms. Diagnosis is confirmed by esophagrams and esophagoscopy to secure a biopsy for histologic proof.

TREATMENT

Carcoma of the esophagus was invariably fatal until Harrington[5] first successfully resected one such growth in 1945. His patient was a woman, aged 60 years, who had increasing dysphagia for a year. Roentgenograms and esophagoscopy revealed an ulcerating polypoid lesion partially obstructing the lower third of the esophagus. A biopsy suggested sarcoma. On June 16, 1945, through a left transthoracic transdiaphragmatic incision, the lower half of the esophagus and cardiac end of the stomach were resected with esophagogastric anastomosis. She was discharged symptom-free 6 weeks after operation. The growth was a leiomyosarcoma. The patient was reported alive and well 7 years later.[6] Another patient described in the same paper, also a woman of 60 years, with a polypoid tumor involving the lower third of the esophagus and cardiac end of the stomach, was found to be inoperable owing to infiltration of the pulmonary vessels, left main bronchus, aorta, and pericardium.

Sweet's[7] patient, with a 4-month history, had a rhabdomyosarcoma resected in July, 1945, when a supra-aortic esophagogastric anastomosis was performed. The patient was an emphysematous, malnourished, arteriosclerotic woman of 78 years who died from pulmonary infection and cardiac failure on the twentieth postoperative day. No metastases were found either at operation or at autopsy.

Lyons and Garlock[8] had a success on April 10, 1946. The patient, 58-year-old woman, had suffered from progressive dysphagia for a year. Roentgenograms showed a large, well-circumscribed tumor involving the middle and lower thirds of the esophagus and projecting into its lumen. Esophagoscopy revealed, at 27 cm., a globular friable mass which biopsy proved to be a leiomyosarcoma.

Through a left transthoracic transdiaphragmatic approach, the growth was resected and an infra-aortic esophagogastric anastomosis performed. The polypoid tumor measured 10 cm. by 4 cm., and had a 5 mm. pedicle. Garlock later reported that while mobilizing this sausage-shaped pedunculated tumor, it disappeared downward into the stomach where it was found near the pylorus. The temptation to remove it locally via a gastrostomy incision was resisted, and wisely so, for subsequent pathologic study revealed that the growth infiltrated the muscular layer of the esophagus in the region of its pedicle, and could only have been adequately removed by formal esophagogastrectomy. It is interesting to note that at the gastroesophageal junction were three nodules, 3 mm. in diameter, which proved to be benign leiomyomas. The patient was well 7 years later.[9]

Clark's[10] patient, a man aged 43 years, was admitted to hospital on Feb. 22, 1947, had an 8-month history of dysphagia, with a 30 pound (13.6 Kg.) weight loss. Esophagrams revealed a large polypoid mass in the upper esophagus, and esophagoscopy confirmed that, at 26 cm. from the upper incisor teeth, there was an irregular grayish-brown firm mass. Biopsy revealed a fibrosarcoma. Through a left thoracotomy, he had an esophagectomy from the cardia to the base of the neck where an anastomosis between the fundus of the stomach and the esophagus was completed. The tumor was 12 cm. long and 4 cm. wide. The patient was well and working one month after operation.

Lortat-Jacob's[11] initial patient, aged 67 years, complaining of dysphagia for 2 months, had a fibrosarcoma 27 cm. from the incisor teeth. Through a left thoracotomy on April 4, 1947, the growth was resected by partial esophagectomy and esophagogastrostomy. He died from a transfusion reaction 3 days later.

On Jan. 3, 1948, his second patient, a man aged 53 years, with a 6-month history of dysphagia due to a growth at the cardia, had partial esophagectomy and an esophagogastric anastomosis. The growth was likewise a fibrosarcoma. This patient died 6 months after operation.

The patient of Brea and associates,[12] admitted to hospital on April 23, 1948, gave a history of progressive dysphagia and 10 Kg. weight loss in 10 months. Esophagrams showed a deformity and displacement at the lower end of the esophagus, and esophagoscopy confirmed narrowing from external compression. Following left thoracotomy, the lesion was found to lie in the lower esophageal wall as a well-circumscribed extramucosal tumor, and was enucleated through a muscle splitting incision. Histologically, it was a fibrosarcoma. Two and a half years later the growth recurred, it proved resistant to radiotherapy and the patient died.

Thorek and Neiman's[3] case was a male aged 43 years, with a 3-month history of dysphagia and an 11 pound weight loss in 8 weeks. Esophagrams showed a filling defect just below the aortic arch, and esophagoscopy a neoplastic lesion 27 cm. from the lower alveolar margin. Biopsy examination suggested a squamous-cell carcinoma. Supra-aortic esophagogastrectomy was performed on Aug. 4, 1948, when a tumor measuring 3.5 by 2.5 by 2.0 cm. was removed. Histopathology revealed a rhabdomyosarcoma of the esophagus.

TABLE I. SARCOMA OF ESOPHAGUS PATIENTS TREATED BY RESECTION

NO.	REPORT	AGE	SEX	DURATION OF SYMPTOMS	DATE OF OPERATION	DATE OF PAPER	TYPE OF LESION	SITE	TYPE OF OPERATION	RESULTS
1.	Harrington	60	F	1 yr.	6/16/45	1949	Leiomyosarcoma; nodular & diffuse	Lower third; ulcerative	L. partial esophagectomy; infra-aortic esophagogastrostomy	Well 7 yr. later
2.	Sweet et al.	78	F	4 mo.	July, 1945	1954	Rhabdomyosarcoma; nodular & diffuse	Mid third	L. partial esophagectomy; supra-aortic esophagogastric anastomosis	Died from pulmonary infection & heart failure, 20th day
3.	Lyons and Garlock	58	F	1 yr.	4/10/46	1951	Leiomyosarcoma	Lower third; polypoid	L. partial esophagectomy; infra-aortic esophagogastrostomy	Reported well 7 yr. later
4.	Clark	43	M	8 mo.	Not stated; adm. 2/22/47	1949	Fibrosarcoma	Middle and upper thirds; polypoid	L. partial esophagectomy; supra-aortic esophagogastrostomy	Working 1 mo. after operation
5.	Lortat-Jacob	67	M	2 mo.	4/ 4/47	1950	Fibrosarcoma	27 cm. from incisor teeth	L. thoracotomy; partial esophagectomy & esophagogastrostomy	Died 3 days post-op., transfusion
6.	Lortat-Jacob	53	M	6 mo.	1/ 3/48	1950	Fibrosarcoma	Lower third	L. partial esophagectomy & esophagogastrostomy	Died 6 mo. after operation
7.	Brea et al.	65	M	10 mo.	4/23/48	1950	Fibrosarcoma; submucosal, no metastases	Lower esophagus	Enucleation	Recurred 2½ years later
8.	Thorek and Neiman	43	M	3 mo.	8/ 4/48	1950	Rhabdomyosarcoma	Middle third; polypoid	Partial-esophagectomy; supra-aortic esophagogastrostomy	Well a year after operation
9.	Maŭro and de Escobar	62	M	1 yr.	8/ 8/48	1951	"Sarcoma polymorphocellular"	Middle third; fungating	Torek type of resection	Died 11th postop. day
10.	Biasini	49	F	1 yr.	11/ 6/48	1949	Fibroleiomyosarcoma	Lower third	Esophagogastrostomy	Satisfactory

11	Gaspar and Bondo	46	M	6 mo	4/ 1/49	1953	Leiomyosarcoma	28 cm from lower incisors	Supraumbilical laparotomy, dilatation of cardia, rt thoracotomy, partial esophagectomy & esophagogastrostomy	Died on 6th postop day, congestive heart failure
12	Michaud	75	M	2 mo	7/23/49	1951	Fibrosarcoma	Cardia	L partial esophagogastrectomy	Original specimen lost, recurrence in 6 mo, biopsy confirmed nature, died 3 mo later
13	Michaud	30	M	2 mo	9/30/50	1951	Leiomyosarcoma	Lower third	L partial esophagectomy and esophagogastrostomy	Satisfactory postop, deep x-ray therapy
14	Owens and Russell	56	F	8 mo	1951	1951	Squamous carcinoma and leiomyosarcoma	Mid third Lower third		Alive & well 25 mo after operation
15	Resano and Hojman	30	M	1 mo	1951	1952	Leiomyosarcoma, diffuse	Upper third, fungating	Wookey procedure	Recovered, no metastases
16	Borrie	63	M	1 mo	4/ 9/52	1958	Fibrosarcoma	Lower third, polypoid	Partial esophagogastrectomy & esophagogastrostomy	Well 6 years after operation
17	Gorbon	65	M	1½ yr	6/30/52	1953	Fibrosarcoma	Lower third	L partial esophagogastrectomy with esophagojejunostomy	Discharged on 18th day
18	Creech et al	62	M	3 mo	6/28/54	1955	Leiomyosarcoma	Lower third	Rt thoracotomy, partial esophagectomy & esophagogastrostomy	Satisfactory
19	DeMuth	54	M	5 wk	7/ 7/55	1956	Rhabdomyosarcoma	Lower third, polypoid	Partial esophagectomy & esophagogastrostomy	Survival

Maũro and de Escobar,[13] in 1951, reported operating on a patient on Aug. 8, 1948, in whom, because of difficulty in defining the limitis of the growth when the esophagus had been freed, a Torek-type of resection was done instead of the usual esophagogastrostomy. The patient died on the eleventh postoperative day from bronchopneumonia.

Biasini's[14] patient, a woman aged 49 years, on Nov. 6, 1948, had resection of a growth in the lower third of the esophagus. On section it proved to be a fibroleiomyosarcoma.

Badosa-Gaspar and Boada,[15] on April 4, 1949, resected an ulcerative leiomyosarcoma of the middle third of the esophagus, measuring 6.5 by 4.5 cm. After preliminary supra-umbilical laparotomy and dilatation of the cardia, they performed a right thoracotomy through the sixth rib bed, followed by partial esophagectomy and esophagogastrostomy. Their patient, however, died on the sixth postoperative day from congestive heart failure.

Michaud's[16] initial patient was a man aged 75 years, who complained of dysphagia and was shown by esophagoscopy and fluoroscopy to have a growth at the cardia. On July 23, 1949, left partial esophagogastrectomy was performed. No histopathologic investigation was later available. Within 6 months the growth recurred, it was then proved to be fibrosarcoma, and the patient died within 3 months. It was therefore assumed that the original lesion was a fibrosarcoma.

His later patient was a man aged 50 years with a lower third growth successfully resected along similar lines on Sept. 30, 1950. As examination showed it to be a leiomyosarcoma, he also received a postoperative course of deep x-ray therapy.

Ovens and Russell,[17] in 1951, reported that their patient, a woman aged 56 years, was admitted to hospital with an 8-month history of dysphagia and 16 pound (7 Kg.) weight loss. Esophagrams revealed a constricting esophageal lesion at the level of the pulmonary vessels and, on esophagoscopy, at 32 cm. from the incisor teeth, a carcinoma was encountered. Through a left thoracotomy, partial esophagectomy with esophagogastric anastomosis was performed. The patient was discharged 28 days later.

Pathologic examination, however, showed the presence of two tumors, one a typical squamous carcinoma in the middle third of the esophagus, and the other, separated from the first by normal esophageal mucosa, was a leiomyosarcoma of the lower end of the esophagus at the junction of the cardio-esophageal mucosa. Neither extended beyond the muscularis nor were any regional lymph nodes invaded. The patient was alive and well 25 months postoperatively.

Burnett and St. John's[18] case, called by them a melanosarcoma, is clearly a true melanoma, and is excluded from this survey of sarcomas.

Resano and Hojman's[19] patient, a man aged 50 years, in 1951 gave a month's history of dysphagia. A vegetating growth at 20 cm. from the incisor teeth was shown to be a leiomyosarcoma. The growth was successfully resected from the cervical esophagus by the Wookey technique.

Gorbon[20] (1953) reported a man aged 65 years, with a growth infiltrating the lower esophagus and cardia, who had successful treatment by partial esophagogastrectomy with esophagojejunostomy on June 30, 1952 He was discharged well 18 days later On histologic examination, the growth proved to be a fibrosarcoma

Creech[21] and associates reported that a 62 year old Negro, with a 3 month history of dysphagia, retrosternal and epigastric pain, with x ray evidence of a polypoid tumor of the lower half of the esophagus, was shown at esophagoscopy to have a pedunculated leiomyosarcoma On June 28, 1954, he had thoracotomy through the right fourth intercostal space There was a freely movable sausage shaped mass within the middle third of the esophagus The esophagus was mobilized from the azygos vein to the diaphragmatic hiatus, the stomach freed through a midline abdominal incision, pyloromyotomy performed and esophagectomy and esophagogastrostomy He was discharged on the fourteenth postoperative day, required dilatation of a stricture 2 months later, and thereafter remained well

DeMuth[22] (1956) reported resecting the second rhabdomyosarcoma in world literature in a Negro aged 54 years The patient gave a 5 week history of difficulty in swallowing solid foods accompanied by the loss of approximately 40 pounds in weight Esophagrams and esophagoscopy revealed a growth 35 cm from the maxillary border and histologic examination proved it to be a rhabdomyosarcoma On July 7, 1955, via a left thoracotomy, partial esophagectomy with esophagogastric anastomosis was performed He was discharged on the nineteenth postoperative day

With the following case report, therefore, nineteen esophageal sarcomas treated surgically were available for study They included 7 fibrosarcomas, 7 leiomyosarcomas, 3 rhabdomyosarcomas, one fibroleiomyosarcoma, and one described as "sarcoma polymorphocellular"

CASE REPORT

J F D, aged 63 years, was admitted to Green Lane Hospital, Auckland, on May 17, 1951, for surgical treatment of an hiatal hernia, which esophagrams had shown to extend approximately 5 cm above the diaphragm (Fig 1) Esophagoscopy confirmed reflux but showed no other lesion

Transthoracic hiatal herniorrhaphy was performed on May 23, 1951 The edges of the hiatus *were defined and the hernial orifice found to take three fingers alongside the esophagus* The wall of the stomach and lower esophagus was palpated, but there was no suggestion of any tumor His convalescence was smooth Esophagrams on June 11, 1951, in both the erect and head down positions confirmed a normal esophagus and a satisfactory hiatal repair, and the patient was discharged fit on June 12, 1951

When seen for the first time by the writer on Jan 18, 1952, during a routine follow up examination, he was symptomless, although an esophagram was suggestive of neoplasm (Fig 2) Within 6 weeks he developed dysphagia, which took the form of a sharp pain behind the lower end of the sternum on swallowing Esophagrams on March 26, 1952, revealed a constant, large irregular filling defect lying in the lower third of the esophagus The barium flowed unobstructed and in a thin stream over the surface of the mass, suggesting the presence of a single polypoid tumor (Fig 3)

The esophagus was next fully mobilized up to the level of the inferior pulmonary vein It was transected well above the growth, and the specimen was

He was readmitted to hospital on April 1, 1952. An esophagoscope passed easily into the stomach and, as the instrument was withdrawn to 40 cm. from the upper jaw, the smooth surface of the growth was clearly seen on the posterior esophageal wall. The growth was estimated to measure 2.5 by 2.0 cm. When a biopsy was taken, the lesion bled freely. Initial histologic examination suggested an anaplastic carcinoma.

Operation.—On April 9, 1952, transthoracic partial esophagogastrectomy was performed by the writer. The technical details follow.

The left chest was opened through the left ninth intercostal space. Adhesions between the base of the left lung and dome of the diaphragm from the previous operation were divided, as was the left pulmonary ligament. The parietal pleura from over the aorta beside the lower third of the esophagus was mobilized, reflected medially, the lower third of the esophagus was isolated, and a catheter sling passed around it.

The abdomen was next opened through a radial diaphragmatic incision. No palpable metastases were detected in the liver, stomach, pelvis, or regional lymph nodes. The growth could be felt lying in the lumen of the lower third of the esophagus. It was decided to perform a block resection of the lesion as described by Allison and the writer.[23]

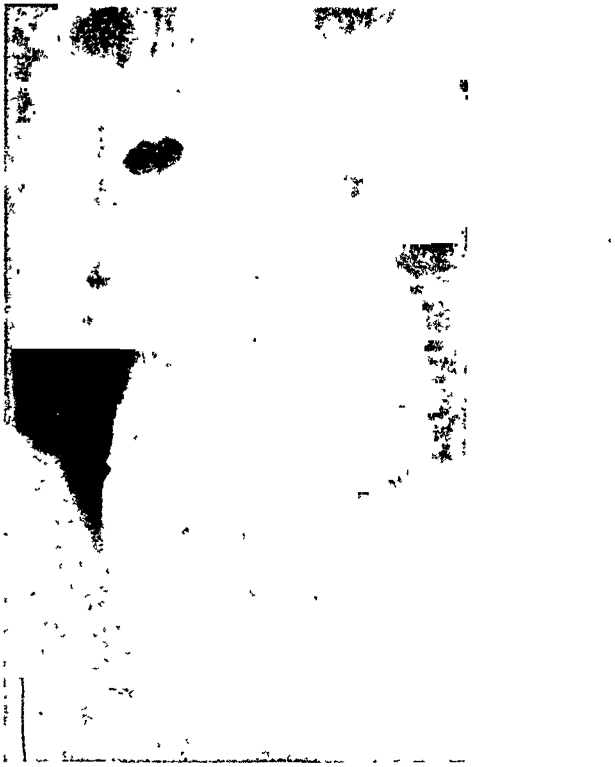

Fig. 1.—Esophagram of May 22, 1951, showing an hiatal hernia.

An incision was made to the left of the spleen in the plane of zygosis between spleen and body of pancreas on the one hand, and dorsal abdominal wall on the other side. The stomach bed was next mobilized medially. The great omentum was divided from the transverse colon. The collar of diaphragm was taken from around a tightly repaired hiatus. The splenic artery and vein were divided, and the pancreas transected at the junction of neck and body. The stump was buried in residual soft tissue. The left gastric artery was next ligated and divided. The stomach was obliquely transected from the greater curvature down to the lesser curvature, thereby removing the proximal half of stomach and the lymphatic sump around the left gastric artery. The lower half of the stomach was completely closed with two layers of continuous chromic catgut sutures.

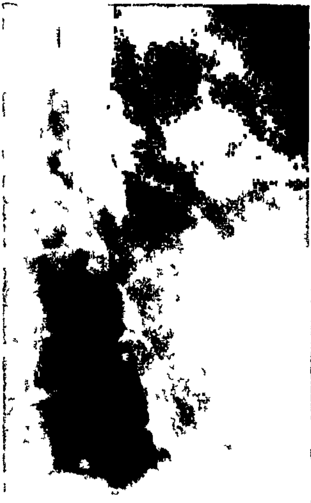

Fig 2

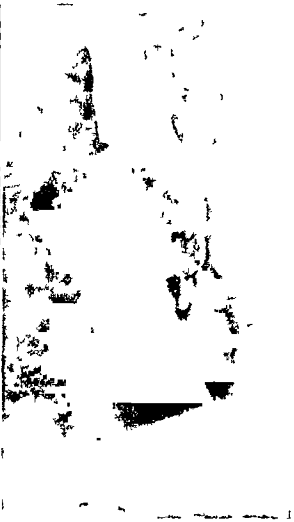

Fig 3

Fig 2—Esophagram of Jan 23 1952 suggesting neoplasm in the lower third of the esophagus

Fig 3—Esophagram of March 26 1952 showing a constant large irregular filling defect in the lower third of the esophagus

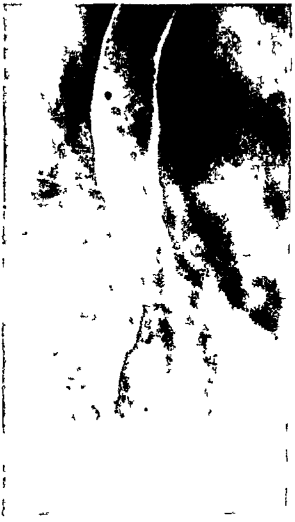

Fig 4—Esophagram on May 6 1952—27 days after operation—showing intrathoracic esophagogastrostomy

Through a seventh intercostal space incision, a two-layer subaortic anastomosis was made between the distal half of the stomach and midesophagus, using interrupted chromic catgut sutures. Some omental tissue was lightly sutured around the anastomosis. The diaphragm was loosely approximated around the stomach, and the remaining diaphragmatic tissue was closed with interrupted sutures. The left lung was inflated and the chest closed in layers over water-seal drainage.

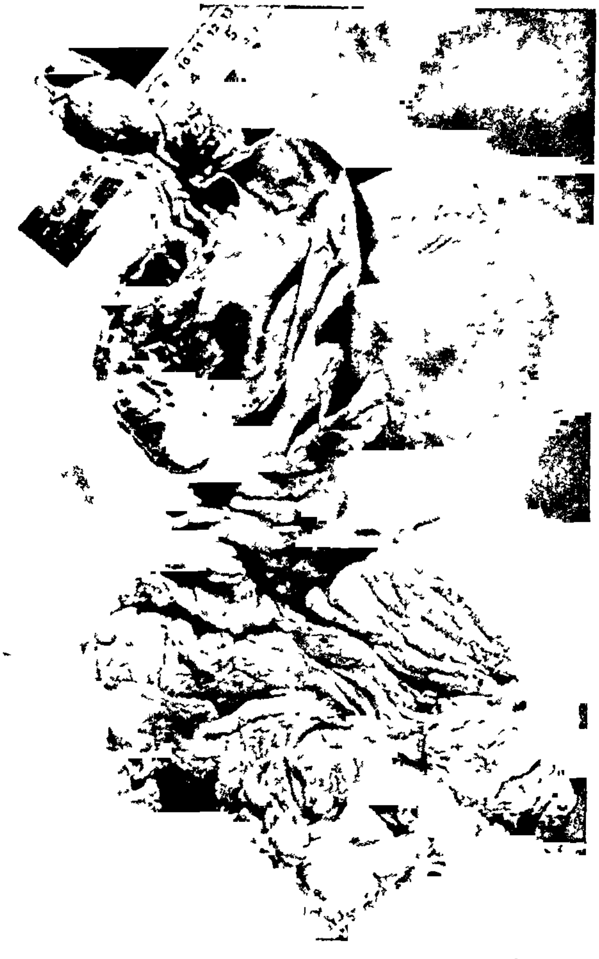

Fig. 5.—Specimen consisting of the lower third of the esophagus and polypoid tumor (lying on the rule) together with the proximal half of the stomach, stomach bed, spleen, omenta, and left half of pancreas.

Progress.—The patient's convalescence was uneventful. He took sips of water by mouth after 24 hours, 1 ounce of water per hour on the second day, he doubled this diet on the third day, and took fluid drinks until the tenth day. Thereafter, he took a light diet, progressed to solid food, and esophagrams made on May 6 showed a satisfactory esophago gastric junction. He was discharged fit on May 7, 1952, 28 days after operation.

Follow-up (Courtesy Mr. David Cole).—On May 10, 1957, although thin, he was well, had no pain, no dysphagia, no flatulence, nor regurgitation. There were no clinical signs of recurrence. Recent esophagrams showed that the anastomosis function satisfactorily, and there was no delay to the passage of thick or thin barium. On May 7, 1958, 6 years after operation, he remained well.

Pathology (Courtesy Dr. Stephen Williams).—(Fig. 5) The specimen consists of the lower one third of the esophagus (8 cm. in length), the stomach, the spleen, the left half of the pancreas, and the omentum. A fringe of diaphragm is attached to the specimen at the cardio esophageal junction, showing a healed, repaired hiatus. Situated in the esophagus there is a somewhat pedunculated oval tumor, measuring 4.0 by 2.8 by 2.0 cm., attached by a broad base to the posterolateral wall of the esophagus. The upper line of excision in the esophagus is 3.0 cm. from the upper pole of the tumor. The tumor is a firm, finely lobulated, grayish mass showing some superficial ulceration and exudation. No enlarged lymph nodes are found in the specimen, but several small nodes lying in the paraesophageal mediastinal tissues are revealed by section. There is no evidence of metastic involvement.

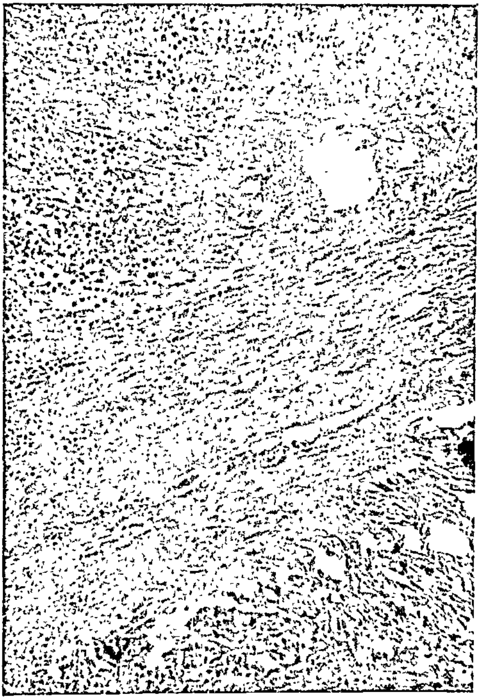

Fig. 6.—Photomicrograph (low power) of the lesion, confirming fibrosarcoma.

Histology.—(Fig. 6) Blocks were taken from the tumor, from two representative lymph nodes, and from the esophagus at the upper line of excision. These show the tumor to be a moderately well-differentiated fibrosarcoma composed of irregular spindle-shaped cells, arranged in sheets lying in different planes. The nuclei show considerable variation of size and shape and include numerous mitoses. The surface layers of the tumors are necrotic and acutely inflamed. A Van Gieson stain confirms the fibrous nature of the tumor, which infiltrates the esophageal wall, penetrating the muscularis mucosa, but not involving the muscle layers. In the submucosa, the tumor tissue becomes continuous with an abnormal development of dense fibrous tissue, presumably scar tissue from previous ulceration.

The esophagus at the line of excision and both lymph nodes show no evidence of malignant infiltration.

The diagnosis therefore is a fibrosarcoma of the esophagus
dense submucous scar tissue. There is no evidence of local meta

DISCUSSION

In the writer's experience, dysphagia after hiatal herniorrhaphy is not uncommon. It is usually acute in onset, arising within a month of operation, and almost always due to a bolus of poorly chewed food plugging the esophageal lumen at the level of the tightened hiatal orifice. Occasionally, it has been due to a fibrous esophageal stricture developing secondarily to the preoperative reflux esophagitis.

The delay in onset of postoperative dysphagia, in this case report, for 8 months after successful hiatal herniorrhaphy is long for such benign causes. It underlines again the fundamental surgical principle that dysphagia, no matter when it arises, be it an initial symptom or one after a successful esophageal operation, cannot be ignored, and that the patient requires prompt, careful, and complete investigation by both esophagrams and esophagoscopy to establish the cause. The one without the other tells only half the story. As the evidence of the esophagrams of January, 1952, was not fully appreciated and, as at that time there was no dysphagia, esophagoscopy was delayed 2 months until the patient's next visit, by which time dysphagia had been present for one month. Had the suggestion of aberration in the January esophagrams been followed up and esophagoscopy performed, the lesion would almost certainly have been detected then.

An analysis of the 19 published surgical cases, found after a thorough review of the world's literature, shows that the ages varied from 43 to 78, with a mean of 58 years. When grouped according to decades, the ages at operation were: 40-49, 4 cases; 50-59, 6 cases; 60-69, 7 cases; and 70-79, 2 cases. Of these, 5 were in females and 14 in males.

The duration of dysphagia varied considerably from one month in the writer's patient, up to 1½ years as reported by Gorbon. Certainly, critical study of those patients having operation does not support the contention of Thorek and Neiman that sufferers from esophageal sarcoma rarely live beyond 6 months. Harrington's patient, with a year of dysphagia, was reported well 7 years later. Lyons and Garlock's patient, alive and well 7 years after resection of a polypoid growth, also had preoperative dysphagia for a year, as did 2 other patients treated surgically.[13, 14]

The pathologic type of the growth need not be a guide to prognosis for, although in the writer's case there was no deep extension from the pedicle of the polypoid sarcoma into the esophageal wall, Harrington reported one, polypoid in type, which had infiltrated widely into the mediastinum when explored.

The site of those lesions treated surgically has varied widely, from one in the upper third of the esophagus, one in both upper and middle thirds, six in the middle third alone, to eleven in the lower third. When present, the x-ray finding of breaking up or "splitting up" of the barium by the growth is a characteristic x-ray feature, as is a peculiar soap-bubble effect, originally described by Allison.[24, 25] Esophagoscopy and biopsy usually establish the true nature of the lesion.

Lower third growths are best treated by the left-sided transthoracic approach with resection and esophagogastrostomy.

Middle and upper third growths may be treated either by the right or left transthoracic approach, according to the surgeon's preference. As with carcinomas, there is an increased operative mortality with these higher lesions.

The patient reported by the writer had block dissection of the regional lymph channels by the technique previously described.[23] although no regional lymph nodal invasion was detected at subsequent pathologic examination, nevertheless the initial satisfactory convalescence and pleasing long-term freedom from recurrence or metastases do lend support to the attitude that in treating neoplasms in the lower third of the esophagus, a deliberate block dissection should be the proper approach to the problem.

The details of pre- and postoperative management follow general lines established for resection of the esophagus for carcinoma.[26]

Four patients died from the effects of operation. As complete long-term follow-up reports of all the remaining 15 cases are not available, it is not possible to generalize on prognosis after operation.

Suffice it to say that, if the patient is otherwise healthy, the lesion localized, and the surgical treatment adequate, the prognosis appears to be good, and that at least 3 patients have now lived more than 6 years after such treatment.

SUMMARY AND CONCLUSIONS

The literature for surgical treatment of sarcoma of the esophagus is briefly reviewed, and a case of polypoid fibrosarcoma of the lower third of the esophagus, discovered 8 months after transthoracic repair of an hiatal hernia and one month after onset of dysphagia, is reported. The patient was treated by partial esophagogastrectomy with esophagogastrostomy and block dissection of the regional lymph nodes. He is alive and well 6 years later.

From an extensive search of the literature, 19 resections for sarcoma of the esophagus were discovered, of which this is chronologically the sixteenth in which surgical treatment was used.

The evidence available suggests that the lesion was not present at the time of the hiatal herniorrhaphy. Its discovery 8 months later emphasizes that esophageal tumors—often symptomless—can and do occur in association with an hiatal hernia, that all patients with hiatal hernias should have a preoperative esophagoscopy, and that recurrence of dysphagia after apparently successful hiatal herniorrhaphy should not be ignored but be promptly, carefully, and repeatedly checked by esophagoscopy as well as esophagrams.

Sarcoma of the esophagus, although rare, should be borne in mind and, if detected early enough and of polypoidal type, it is amenable to successful resection, with an excellent prognosis.

ADDENDUM

The patient remains well 6 years and 9 months after operation.

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I am happy to record my obligation to Mr. Douglas Robb, Surgeon-in-charge, Cardio-Thoracic Unit Green Lane Hospital, Auckland, where the patient was treated, and I gratefully acknowledge photographic help from Mr. Litherland, Medical Photographer, Auckland Hospital, and help in obtaining microfilms of the rarer references by Mr. H. D. Erlam and Miss E. Murray, Medical Library, Medical School, University of Otago, Dunedin. I am indebted to Miss N. Richardson for secretarial help and to Mr. Gerald Brookes, of the University of Otago, for further preparation of the illustrations.

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EPIDERMOID CARCINOMA IN MUCOSA OVERLYING A PEDUNCULATED LIPOMA OF THE ESOPHAGUS

Raul A. Marcial-Rojas, M.D. * *and Pedro Suau, M.D.,***
San Juan, Puerto Rico

THE subject of benign tumors of the esophagus is rapidly dismissed in most textbooks of pathology, medicine, gastroenterology and bronchoesophagology. The descriptions are usually limited to a few sentences, always emphasizing their infrequency, and usually enumerating the several histologic types which have been sporadically reported in the literature. Upon a careful review of the literature, one is impressed with the repetition of the statement that benign neoplasms are extremely rare, there are few recorded cases, thus they deserve very brief mention. In 1926, Vinson and his co-workers[1] mentioned the occurrence of only three benign esophageal tumors among approximately 4,000 patients complaining of dysphagia. Practically all publications deal with individual case reports.[2-16] In 1932 Patterson[11] presented one case and reviewed the literature. He was able to find 61 instances of benign tumors of the esophagus in a period of time extending from 1717 to 1932. He mentioned only two lipomas.

In 1953, Stout and his colleagues[17] classified 103 benign tumors of the esophagus as intraluminal and intramural. The former could be sessile or polypoid and the latter solid or cystic. Most of the polypoid tumors were considered by them to be fibrous polyps secondary to hyperplasia of the subepithelial tissues and to assume their pedunculated structure aided by the action of peristalsis. Some of the polypoid tumors were also lipomas, fibrolipomas, and even leiomyomas. The immense majority of the intramural tumors were leiomyomas.

Malignant degeneration of a benign esophageal tumor is so infrequent as to almost constitute a pathologic curiosity. Feldman[7] reported an adenocarcinoma apparently arising in an adenomatous polyp of the esophagus. Stout and Lattes[18] refuse to accept this case as valid *in view of the fact that only a small* biopsy was performed. We are of the same opinion. Probably the most frequent example of malignant degeneration of a benign esophageal tumor is exemplified by leiomyoma. It constitutes the most frequently encountered benign

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*Professor and Chairman, Department of Pathology, University of Puerto Rico School of Dentistry; Pathologist to Dr. I. González Martínez Oncologic Hospital, San Juan, P. R.

**Assistant Clinical Professor in Surgery, University of Puerto Rico School of Medicine, San Juan, P. R.

tumor of the esophagus and it is possible that some of the leiomyosarcomas may have arisen from previously existent leiomyomas. One of these cases is suggested by Puestow and co-workers.[12] It was a polypoid leiomyosarcoma, and he assumed from the clinical history of long symptomatology that it developed from a pre-existent leiomyoma.

The simultaneous occurrence of benign and malignant tumors of the esophagus is rare.[19] The invasion of a fibrous polyp by an epithelioma is recorded by Targett.[20] Schirmer[21] observed an ulcerating carcinoma in close proximity to a pedunculated lipoma near the cardiac end of the esophagus. Callanan[22] reported, in 1954, the simultaneous occurrence of a small intramural leiomyoma and an overlying squamous-cell carcinoma. He claimed it constituted the first case of this simultaneous occurrence reported in the literature. Puestow[12] in 1955 reported a similar case of squamous-cell carcinoma of the esophagus with an underlying small intramural leiomyoma. An example of an epidermoid carcinoma of the mucosa overlying a pedunculated fibrous polyp is shown by Stout[18] in his fascicle on esophageal tumors.

The purpose of this communication is to report on an instance of a pedunculated esophageal lipoma with an epidermoid carcinoma of the overlying esophageal mucosa. This apparently constitutes the fifth instance in the literature of associated benign and malignant tumors of the esophagus and the second one of a pedunculated lipoma and epidermoid cancer.

CASE REPORT

A 63-year-old white man who had been complaining of a sore throat and slight pain in the left side of the neck for the previous 5 months was admitted to the Presbyterian Hospital for laryngoscopic examination on May 8, 1957. He had visited a physician on several occasions during that period of time. Pathologic changes which could explain the sore throat and the cervical pain were never encountered until his last visit when a nontender, movable mass, 4 cm. in main diameter, was found in the left side of the neck.

The laryngoscopic and nasopharyngoscopic examinations were negative. A slightly suspicious lesion in the left side of the base of the tongue was biopsied. The pathologic examination failed to disclose the presence of neoplasia. A chest film was negative.

On May 22, he had an excisional biopsy of the cervical mass. A frozen section revealed metastatic epidermoid carcinoma in a cervical lymph node. When the patient was recovering from the anesthesia he coughed and a large pedunculated mass protruded from the left angle of the mouth. It showed an ulcerated lesion on its most distal portion. Before anything could be done the patient swallowed the mass again.

A barium meal was given to the patient on May 29 which disclosed a markedly dilated esophagus occupied by a pyriform mass (Fig. 1). The distal portions of the mass were encountered at the level of the cardioesophageal junction. An esophagoscopic examination was performed and the bulk of the tumor was encountered in the distal third with the pedicle attached to the cervical esophagus.

On June 8, a cervical esophagotomy was performed and the polyp was excised at its junction with the cervical esophagus. A frozen section showed the epidermoid carcinoma on the surface of the lipoma at its distal portion. A left radical neck dissection was also performed.

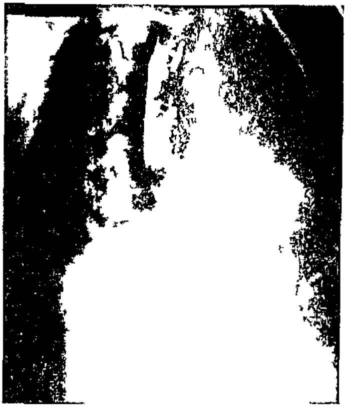

Fig 1—Barium swallow disclosing the marked dilatation of the esophagus by the polypoid tumor The lowermost portion of the tumor rests on the cardioesophageal junction

Fig 2

Fig 3

Fig 2—The polypoid lipoma with the ulcerated epidermoid carcinoma in the overlying mucosa Note the smaller lipoma attached to the same pedicle

Fig 3—The bisected lipoma showing the ulcerated carcinoma infiltrating the most superficial portions

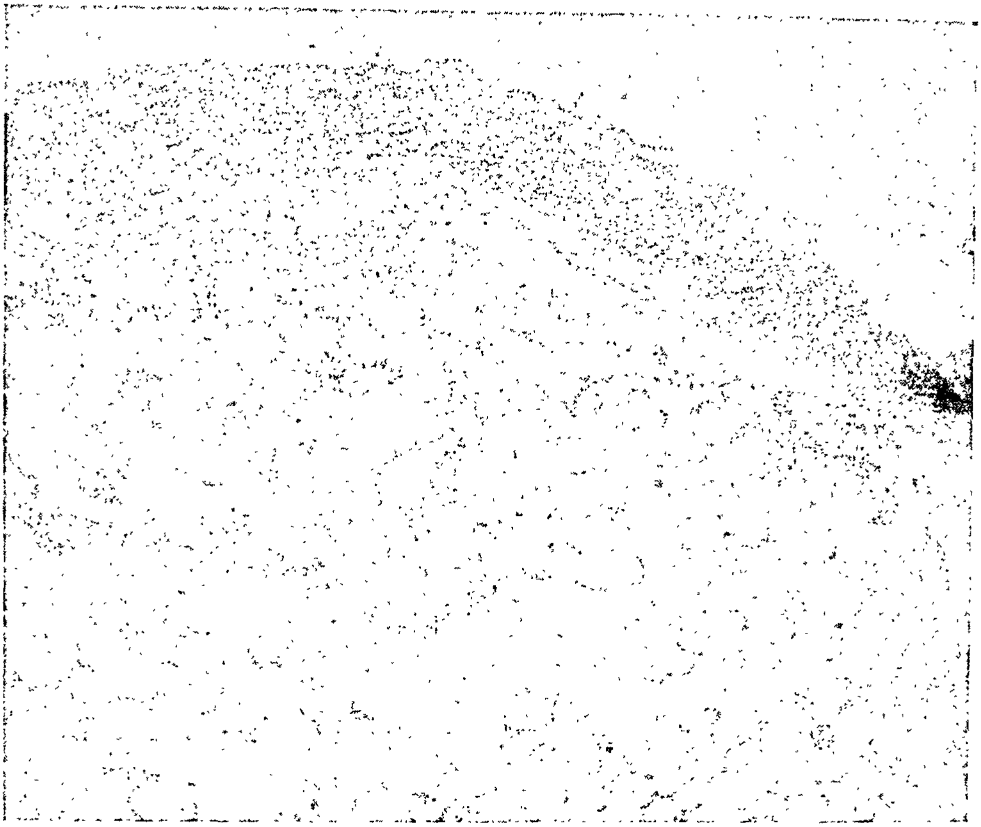

Fig. 4.—Section of the lipoma covered by esophageal mucosa (hematoxylin and eosin; ×100).

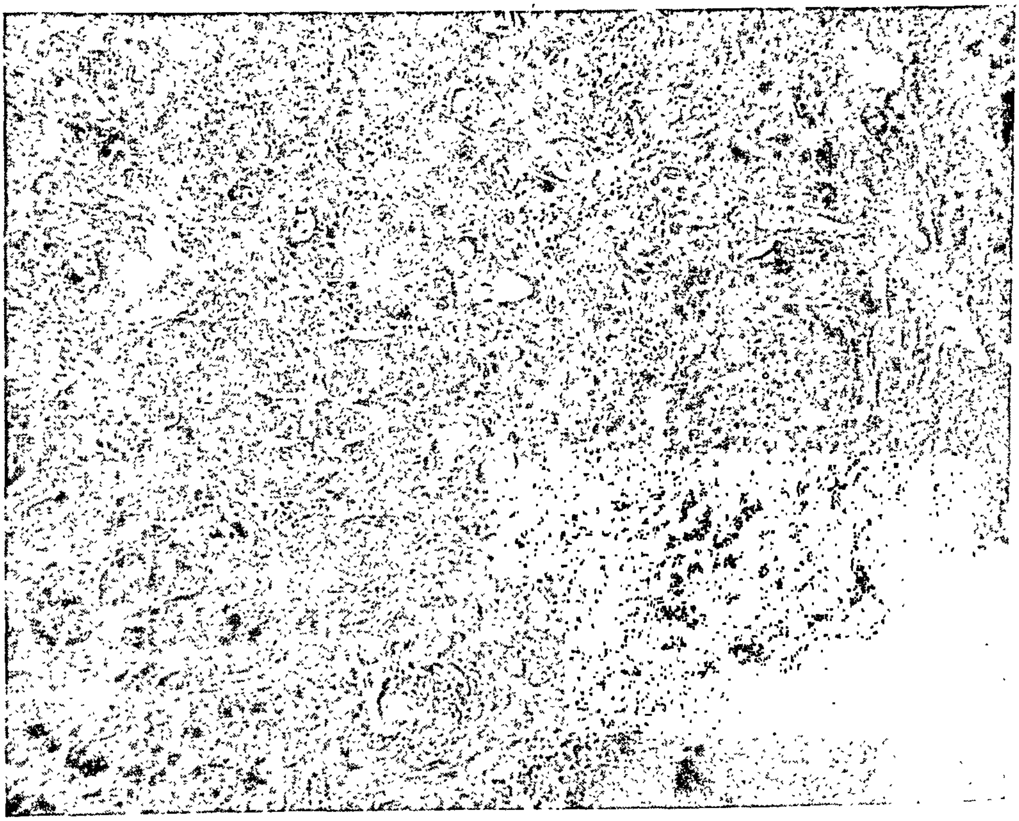

Fig. 5.—Epidermoid carcinoma arising from esophageal mucosa and infiltrating the subepithelial tissues (hematoxylin and eosin; ×360).

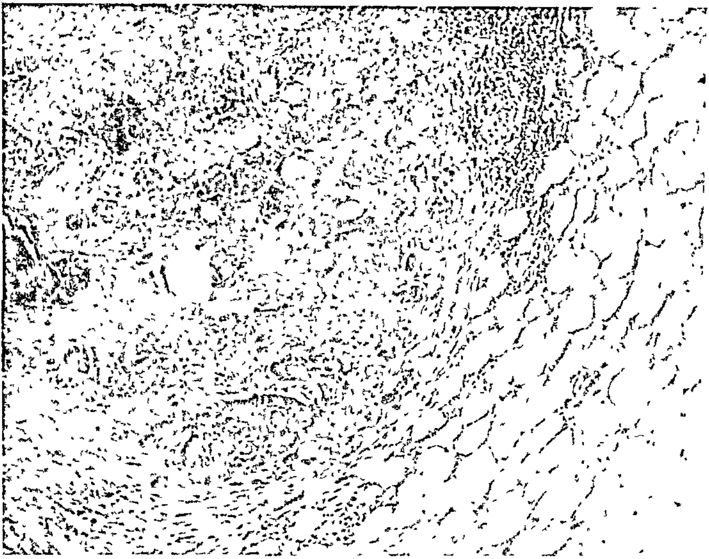

Fig. 6—Epidermoid carcinoma infiltrating into the substance of the lipoma (hematoxylin and eosin; ×360).

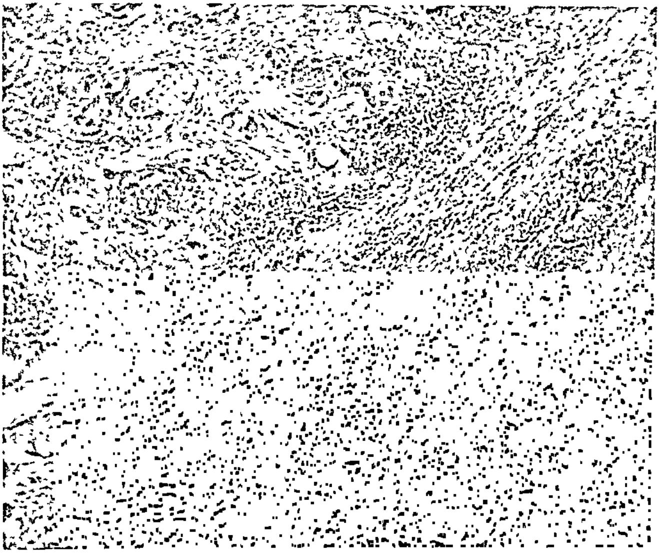

Fig. 7.—Metastatic epidermoid carcinoma in the only affected cervical lymph node (hematoxylin and eosin; ×360).

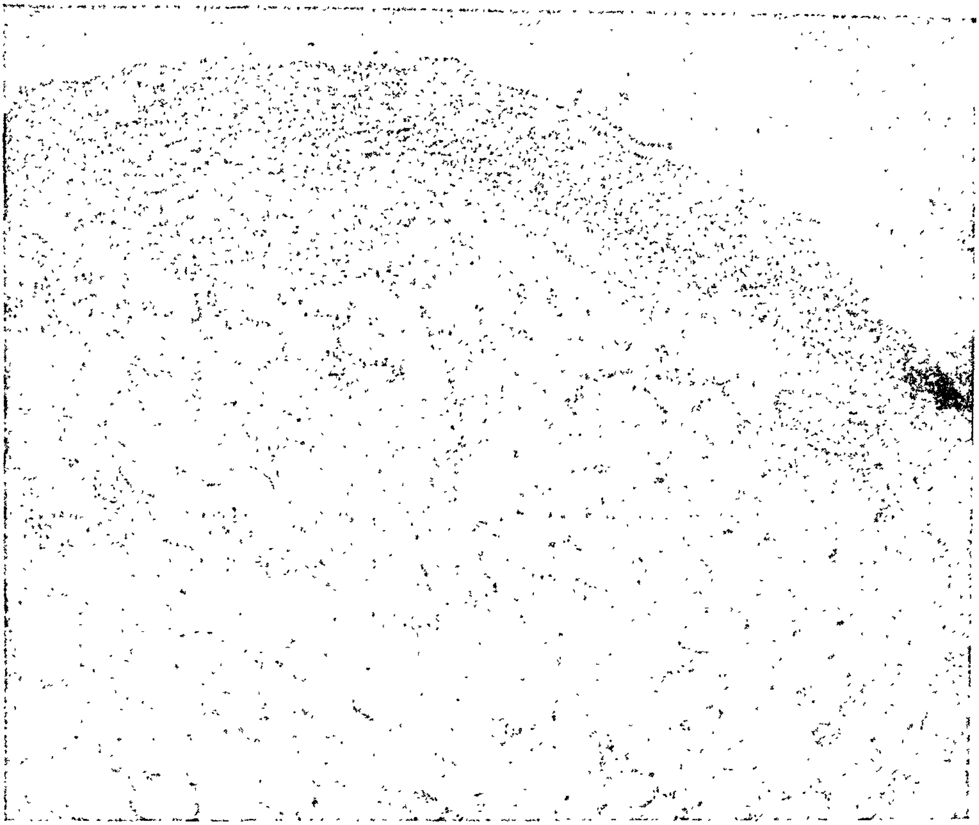

Fig. 4.—Section of the lipoma covered by esophageal mucosa (hematoxylin and eosin; ×100).

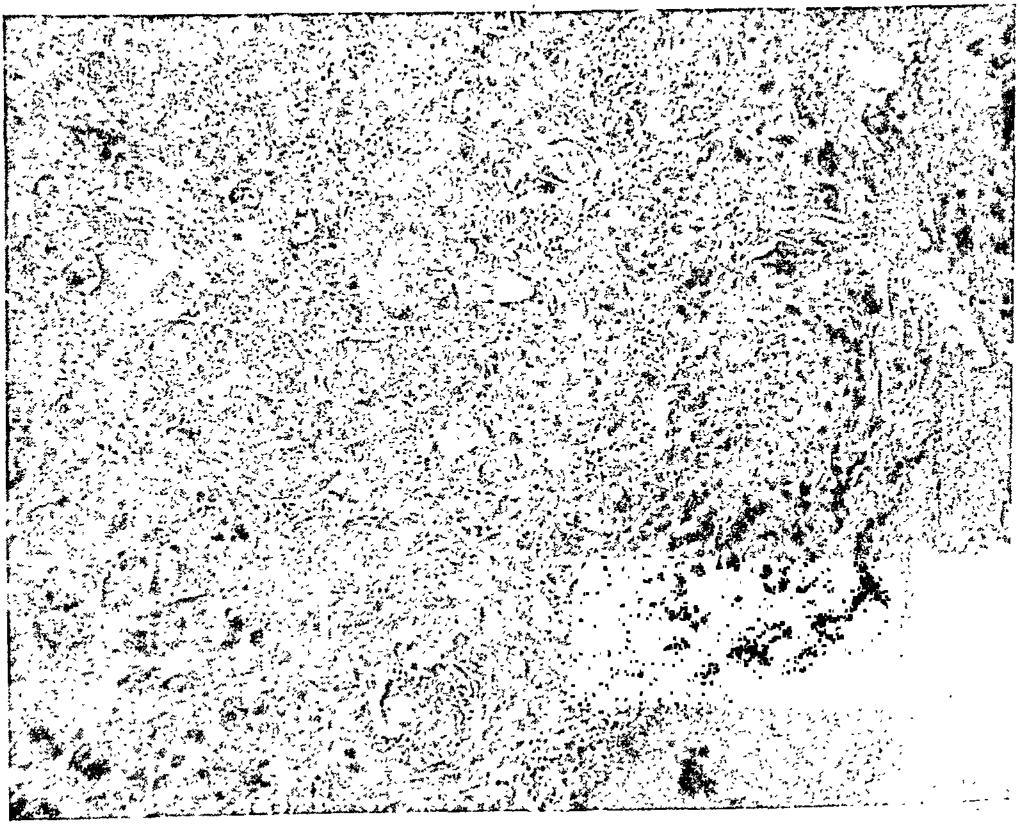

Fig. 5.—Epidermoid carcinoma arising from esophageal mucosa and infiltrating the subepithelial tissues (hematoxylin and eosin; ×360).

The tumor metastasized precociously to one cervical lymph node and recurred at the site of removal of the pedicle in the cervical esophagus As multiple sections of the lipoma through the pedicle failed to disclose carcinoma we must postulate with reasonable certainty that, when the pedicle was ligated at the cervical esophagus, a tumor embolus must have been caught in transit to the cervical lymph nodes and was retained there by the suture

The case also emphasizes the fact that no matter how minimal is the symptomatology referable to the esophagus in a case of metastatic carcinoma to cervical lymph nodes of unknown origin, a barium swallow and even an esophagoscopy should be done as part of the routine procedure to detect the concealed lesion

SUMMARY

1 A review on the subject of benign tumors of the esophagus with particular interest in the simultaneous occurrence of benign and malignant lesions has been presented

2 The case represents the fifth instance of this simultaneous occurrence of benign and malignant tumors of the esophagus and the second one of a pedunculated lipoma and an epidermoid carcinoma

The authors are most grateful to Dr Jose Nova Benitez, Professor of Surgery of the University of Puerto Rico Medical School, and to Dr Jose Pico, Professor of Otorhinolaryngology of the same institution, for their valuable help and advice in the management of this case

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Pathologic Findings.—

Gross description: The polypoid mass measured 11 by 3.5 cm. and was covered for the most part by normal esophageal mucosa (Fig. 2). A smaller but similar mass was attached to its pedicle and measured 3 by 1.5 cm. On cut surface, both the large and small polypoid masses were composed of yellowish adipose tissue with minimal areas of fibrosis (Fig. 3). The esophageal mucosa covered both pedunculated lipomas except for an ulceration on the distal and anterior portions of the larger one. This ulcer measured 2.5 by 1.5 cm. and beneath it the subepithelial tissues were infiltrated by grayish-white neoplastic tissue for a distance of 2 mm. The contents of the radical neck dissection were carefully studied and 28 lymph nodes were recovered. None of them showed metastatic carcinoma.

Microscopic description: The polypoid tumors were pedunculated lipomas with some areas of fibrosis (Fig. 4). The ulcerated lesion was an epidermoid carcinoma, grade 2, which infiltrated the subepithelial tissues and the substance of the lipoma (Figs. 5 and 6). The line of resection at the pedicle was free of tumor. It is of interest to note that none of the cervical lymph nodes showed metastatic tumor. Apparently the only lymph node affected was the one removed for biopsy (Fig. 7).

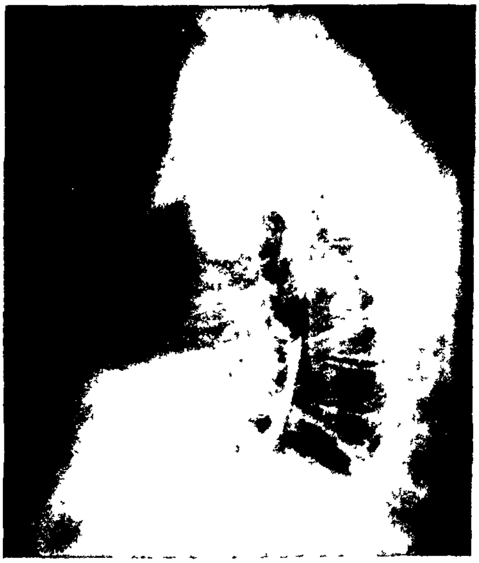

Fig. 8.—Barium swallow shows the area of stenosis at the cervical esophagus due to persistent carcinoma.

The patient recovered very nicely from the surgical procedure except for a small salivary fistula that healed spontaneously. Four months after the operation he was re-admitted to the hospital because of progressive dysphagia and sialorrhea. A barium swallow disclosed an area of stenosis at the site where the polypoid mass had been removed from the cervical esophagus (Fig. 8). The possibility of scarring and stenosis was considered. A biopsy from that area revealed an epidermoid carcinoma of similar histology as that found on the pedunculated lipoma. The patient was submitted to radiotherapy. A gastrostomy had to be performed as the disease progressed rapidly and became uncontrollable. The last time that the patient was seen he was deteriorating rapidly and showed obvious clinical evidence of persistent disease.

DISCUSSION

This is a most unusual case of the simultaneous occurrence of a benign and a malignant tumor of the esophagus. An infiltrating epidermoid carcinoma developed in the mucosa overlying a pedunculated lipoma of the esophagus.

The tumor metastasized precociously to one cervical lymph node and recurred at the site of removal of the pedicle in the cervical esophagus As multiple sections of the lipoma through the pedicle failed to disclose carcinoma we must postulate with reasonable certainty that, when the pedicle was ligated at the cervical esophagus, a tumor embolus must have been caught in transit to the cervical lymph nodes and was retained there by the suture

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"AIR PLOMBAGE" WITH RESECTION FOR PULMONARY TUBERCULOSIS: A TECHNIQUE FOR DECREASING COMPLICATIONS

James W. Pate, M.D., Felix A. Hughes, Jr., M D , Roger E. Campbell, M.D., and John M. Reisser, M.D., Memphis, Tenn.

The complication rate following pulmonary resection for tuberculosis is disturbingly high, although the mortality is low (about 0.5 per cent). In an attempt to find a practical method of lowering the complication rate, 61 upper lobe pulmonary resections for tuberculosis with concomitant "air plombage" were performed and this group is contrasted with a series of 313 consecutive upper lobe resections for tuberculosis not accompanied by any collapse procedure.

Numerous different techniques have been tried in an attempt to prevent complications after pulmonary resections. In 1953, Chamberlain[1] mentioned the use of "extraperiosteal plombage of the patient's subscapular collection of blood" in a few segmental resections. Since then, we have used a similar technique, which we call "air plombage" in some of our cases. A search of the literature has failed to reveal an evaluation of this procedure.

TECHNIQUE

Distribution of the two groups is shown in Tables I and II.

After the pulmonary resection is completed and the intrapleural tubes are in place, the pleura and intercostal muscles and fascia are closed in the routine manner. An estimate is made, before closing, of the amount of lung tissue removed, the location and shape of the remaining lung and the degree of pleural filling which the lung will easily assume without overexpansion. If the remaining lung does not fill the pleural space with ease, or if large raw surfaces remain in a plane which cannot easily contact the chest wall, or if there is an excessive air leak from the parenchyma, the decision to do an air plombage is made. Portions of the first, second, third, and usually the fourth ribs are stripped subperiosteally, leaving attached periosteum on their outer surfaces. The size, shape, and location of the resultant pocket is made to fill

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From the Thoracic Surgery Section, Surgical Service, Veterans Administration Medical Teaching Group Hospital, Memphis 15, Tenn

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the defect left by the pulmonary resection. The pleura, periosteum, and intercostal muscles and facia drop in to contact the resected surface of the lung. No drainage of this space is done. The chest wall is then closed in anatomic layers.

After surgery, the air pocket will slowly fill with blood and fibrin. It will decrease in size as the lung heals and the pleura will be pushed up by the expanding lung until little if any evidence of the plombage remains (Figs. 1 and 2).

TABLE I

	WITHOUT AIR PLOMBAGE	WITH AIR PLOMBAGE	TOTAL
Lobectomy	116	32	148
Segmental	123	22	145
Wedge	74	7	81
Total	313	61	374

TABLE II

SEGMENTS REMOVED	WITHOUT AIR PLOMBAGE PER CENT	WITH AIR PLOMBAGE PER CENT	TOTAL PER CENT
Apical	13.9	3.3	17.2
Apicoposterior	26.0	4.2	30.2
Lobectomy	36.8	5.3	42.1
Posterior	4.7	0.9	5.6
Apicoposterior and superior	3.9	0.3	4.2
Total	85.3	14.0	

RESULTS

A comparison of the complication rates in the two series is presented in Table III. There was only one death (0.3 per cent) in the entire group, and that due to myocardial infarction.

TABLE III. COMPLICATIONS

	OPERATION			
	LOBE	SEGMENT	WEDGE	TOTAL
	Without Air Plombage			
Number of cases	116	123	74	313
Number of complications	24	28	8	60
% Complications	20.7	22.8	10.8	19.3
	With Air Plombage			
Number of cases	32	22	7	61
Number of complications	1	0	0	1
% Complications	3	0	0	1.6

The complication rates were high, but this is due to the fact that (1) only upper lobe surgery is analyzed here (the rate for middle and lower lobe resections is lower), (2) all complications are included ("residual air space" of more than 2 weeks' duration is considered to be proof of a bronchopleural fistula), (3) only 30.8 per cent of the patients were original treatment cases, (4)

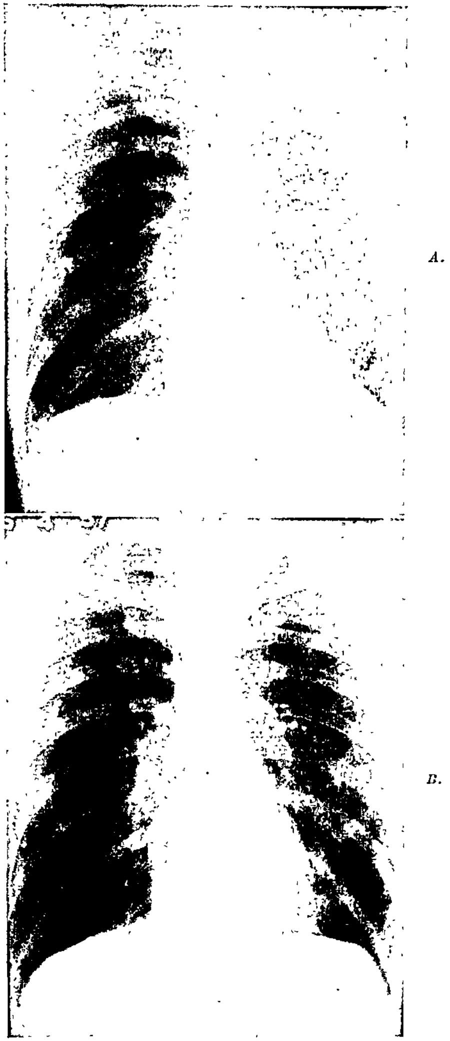

Fig. 1.—*A*, X-ray of chest 4 days after a left upper lobectomy and air plombage. *B*, X-ray of same patient 10 months later.

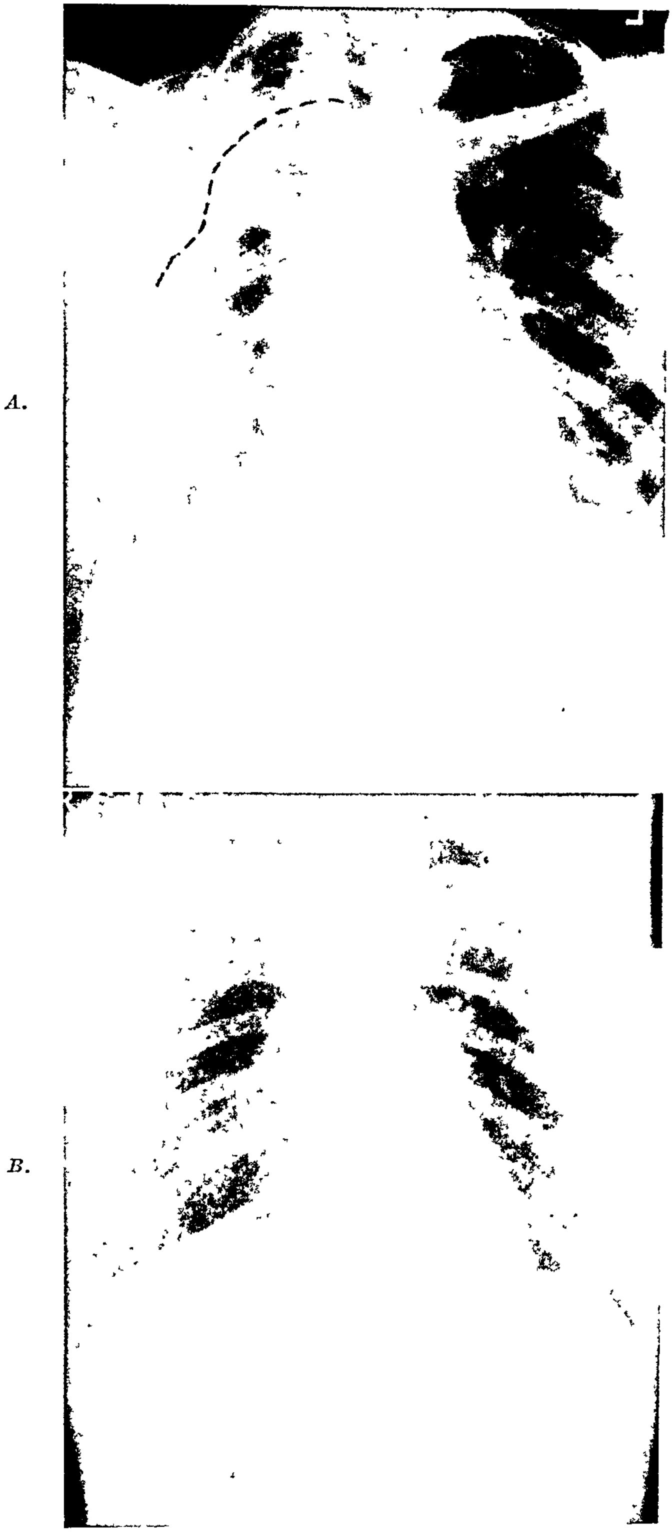

Fig. 2.—*A*, X-ray of chest one day after a right upper lobectomy and a large air plombage. The dotted line shows the edge of the plombage space. *B*, X-ray of the same patient 3 months later.

70 per cent of the patients had open cavities resected (there were few "nubbins" removed), (5) 17 2 per cent of the patients had had previous major chest surgery, and (6) 76 3 per cent gave positive sputa within 3 months prior to surgery

The complication rate was quite different in the two series The difference between a total complication rate of 19 3 per cent and a rate of 1 6 per cent is statistically significant and clinically impressive The statistical comparison is further emphasized by the number of postresection thoracoplasties required to deal with fistulas, empyema, etc

Forty one (13 per cent) of the patients with resections unaccompanied by air plombage required later thoracoplasty to deal successfully with complications An additional 3 patients had subsequent decortication Thus, a total of 14 per cent of this group required later major surgery to handle the complications of pulmonary resection On the contrary, only one (1 6 per cent) of the patients with resection who had air plombage required thoracoplasty, and none, decortication

The complication rate for apical and posterior segmental resection was 15 per cent Upper lobectomy gave the same incidence of complications Apical segmental resection was followed by complications in 8 5 per cent, and apical posterior superior lower lobe resections produced 7 per cent complications Posterior segment resection alone was followed by complications in 3 of 16 cases and apical superior segment in 2 of 3 cases The only complication in the group with air plombage was in a right upper lobectomy with anomalous arterial supply (Table IV)

TABLE IV TYPES OF COMPLICATIONS
(CASES WITHOUT AIR PLOMBAGE)

	OPERATION				
	LOBE	SEGMENT	WEDGE	TOTAL	PER CENT
Bronchopleural fistula	13	14	3	30	9 5
Empyema	1	5	1	7	2 2
Spread	2	1	0	3	0 9
Hemorrhage	5	3	0	8	2 5
Tuberculous wound infection	1	1	0	2	0 6
Others	8	5	4	17	5 2
Total	30	29	8	67	21 2

Note Some patients had more than one complication

From these figures it appears that air plombage is especially valuable in resections involving the apical and posterior segments and in upper lobectomy It is of some value when either the apical or posterior segment alone is resected

We believe that a resection involving one or more segments of the upper lobe along the superior segment of the lower is especially vulnerable to complications, and that, therefore, air plombage is indicated in this group

DISCUSSION

Bronchopleural fistula (or "residual air space") remains the most frequent and one of the most troublesome of the complications of pulmonary resections This is especially true following surgery on the upper lobe, particularly in tuberculosis patients

Several factors appear to lead to an increase in incidence of fistula. These include: (1) *Active disease* at the line of resection. (2) *Technical errors* in dealing with the lung tissue (this seems to be in regard to the minute bronchi in the parenchyma rather than the bronchial stump itself). (3) *Dead space* due to fibrosis in the lung with decreased compliance preventing the lung from filling the pleural space; or a total air leak (usually in the lung surface) sufficiently large to prevent a negative intrapleural pressure from expanding the lung; or a gross discrepancy in the shape of the intrapleural space and the lung surface, causing air pockets to be trapped, such as in the apex after an apical segmental resection.

Air plombage was developed to prevent the formation of an intrapleural pocket of dead space. If properly performed it does this in several ways. First, it allows relatively healthy tissue to fall against the raw surface at the line of resection. This tends to seal multiple minute air leaks, and aids healing by preventing overexpansion which may result in persistent leaks and active disease. Second, it gives the chest wall a controlled amount of flexibility, thus preventing an excessive intrapleural negative pressure during forced or rapid inspiration, which tends to keep small bronchi open. Third, the procedure "tailors" the shape of the intrapleural space to fit that of the lung so that a fibrosed or noncompliant lung with abnormal shape resulting from resection will touch the pleura at all points and most importantly at its raw surface, thus obliterating the pleural space.

A satisfactory air plombage must (1) result in an extrapleural pocket of about the same volume as the resected pulmonary tissue, and (2) be so located that the shape of the intrapleural space is the same as that of the remaining lung surface.

Needless to say, the stripped portion of the chest wall must be intact to prevent intrapleural contamination from entering the space with resultant infection.

While these same factors may be produced by a concomitant thoracoplasty (with about the same results), air plombage has several additional advantages. First, it results in no bony deformity or scoliosis; second, it is faster and less traumatic than thoracoplasty; third, it is somewhat automatically reversible. for, after all air leaks are sealed and the raw surface is healed, the lung will expand, pushing the stripped area back against the ribs and thus obliterating the space. Fourth, the presence of blood, fibrin, and trapped air in a closed space covered by the bony cage will prevent excess paradoxical motion even when a large space is created. This allows a much larger stripping with a greatly simplified postoperative course than would be obtained with a thoracoplasty.

SUMMARY

1. A group of 61 upper lobe resections with concomitant air plombage is compared with 313 upper lobe resections without a collapse procedure.

2 The *over all* complication rate was 19 3 per cent in the group without air plombage, but only 1 6 per cent in the group in which air plombage was done

3 Without a concomitant collapse procedure, 14 per cent of the patients required further surgery for the treatment of complications contrasted with only 1 6 per cent of the group with air plombage

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SPACE PROBLEMS IN EXTENSIVE RESECTION FOR PULMONARY TUBERCULOSIS: THE USE OF PRE-RESECTION TAILORING THORACOPLASTY

Frank J. Milloy, M.D., Ahmed Kahdem, M.D., and Hiram T. Langston, M.D., Chicago, Ill.*

THE ANATOMIC distribution of pulmonary tuberculosis is frequently such that extensive resection of the upper portion of the lung is necessary. One of the requirements for success in these segmental or lobar resections is that the remaining pulmonary tissue be capable of filling the pleural space. If this requirement is not met, an unfilled space results which may well become the location of an empyema.

In a recent report, Bell[1] found 30 instances of postresection space problems in 135 lobectomies, an incidence of 22 per cent. Wareham and his co-workers[5] found, in a group of 55 lobectomies, twelve persistent pleural spaces, an incidence of 20 per cent and, in a group of 22 patients who underwent lobectomy plus segmentectomy or wedge resection, nine persistent pleural spaces, an incidence of 40 per cent. Although, they emphasized that some of these spaces remained uncomplicated, many required further surgical intervention.

The space resulting from resection of a portion of the lung is ordinarily obliterated by one or both of two processes. These are overexpansion of the remaining lung tissue and decrease in the size of the hemithorax. Decrease in the size of the hemithorax is produced physiologically by mediastinal shift, narrowing of the intercostal spaces, and/or a rise in the level of the diaphragm. If these physiologic compensatory mechanisms are insufficient, surgical measures may be taken to decrease the size of the hemithorax, such as paralysis of the diaphragm, creation of a "pleural tent," or the performance of some type of thoracoplasty.

If thoracoplasty is required as an adjunct to pulmonary resection, it may be performed (1) concomitant with resection, (2) following the resection, or (3) preceding resection.

1. *Concomitant Thoracoplasty.*—In most of the patients operated upon in this institution there has been severe apical disease with dense pleural adhesions, and we have frequently found it necessary to use extrapleural and

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From the Chicago State Tuberculosis Sanitarium and Department of Surgery, University of Illinois, Chicago, Ill.

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*Special Fellow of the World Health Organization sponsored by the American College of Chest Physicians.

extrafacial planes of dissection over wide expanses of the chest wall. To resect upper ribs, in the face of extrapleural dissection at the apex, would leave little more than shreds of intercostal tissue representing the upper chest wall. Likewise, there is no tissue locally from which to construct a "pleural tent." Even without this set of circumstances, we feel that the added burden of paradoxical motion in the chest wall should be avoided if possible, since it undoubtedly increases the morbidity, particularly when added to an extensive pulmonary resection. Thus, we rarely consider concomitant thoracoplasty.

2. *Postresection Thoracoplasty.*—Since one cannot be positive that a serious space problem will necessarily develop following any given resection, it can be argued that it is reasonable to carry out the indicated resection, however extensive it may be, and hope for full and complete pulmonary expansion. Any space or empyema that may result is then treated by needle aspiration, tube drainage, or thoracoplasty as indicated. This approach has the disadvantage of allowing a complication to develop which might have been prevented.

3. *Preresection Thoracoplasty.*—In advocating a preresection thoracoplasty, we subscribe to the tenet that by careful evaluation the exact extent of the resection to be performed, or at least its maximal and minimal limits, can be clearly determined. The anatomic extent of involvement is estimated by review of all available x-ray films as well as by other methods of examination which include bronchoscopy, bronchography, and laminography.

The lateral laminogram is often particularly helpful in determining whether there may be significant residual disease in the middle lobe or in the superior segments of the lower lobes. Likewise, a great deal may be learned concerning inflammatory changes of the bronchial tree and possible distortions of the spacial relationships between segments and lobes, in these cases, by means of routine bronchography.

Physiologic evaluation, including bronchospirometry as well as determination of pulmonary artery pressures by right heart catheterization, permits a more complete classification of the patient in regard to surgical risk.

We are further influenced by clinical factors, such as the presence of contralateral disease, which might impose limitations on extent of resection on the one hand, or by drug resistance on the part of the organism which might argue for wider resection on the other hand.

Due allowance is made, of course, for the patient whose disease has already so contracted a large extent of lung parenchyma over a chronic course that the volume of lung to be removed is small, in spite of the total number of lung segments involved. Under these circumstances, compensation has already been largely effected for the tissue to be removed and a space-reducing procedure may not be necessary.

After consideration of all these factors, we have adopted the policy of performing a preliminary tailoring thoracoplasty if it is expected that the proposed resection will consist of an amount of lung greater than the volume of one lobe but less than a total pneumonectomy.

TECHNIQUE

Preliminary tailoring thoracoplasty, as we use it, is carried out some 3 or more weeks before the pulmonary resection. It consists of subperiosteal removal of the first rib from the tip of the transverse process to the costochondral junction and of most of the second and third ribs from the tips of the transverse processes to a point anteriorly just short of the costochondral junction.

Our purpose is to shorten the superior inferior axis of the chest, since this appears to be the critical diameter. Consequently, there is no advantage in resecting the second and third ribs beyond the point that is on a horizontal level with the posterior portion of the fourth rib.

Further, an apicolysis may be performed which tends to ensure that the pleural dome is dropped to the level of the fourth rib posteriorly and the stumps of the second and third ribs anteriorly. Even though this level of the pleural dome achieved by apicolysis may not be a permanent one, it appears at times to have the advantage of reducing further the vertical diameter of the hemithorax, particularly in the gutter.

At the subsequent thoracotomy, the chest is entered through the bed of the fifth rib. If added collapse is required, a five-rib thoracoplasty of tailoring type can be had by the resection of an appropriate length of the fourth rib. If this is not necessary, the hemithoracic volume is not affected beyond the original three-rib procedure.

MATERIAL AND RESULTS

In the past 4 years, 31 patients have undergone pulmonary resection of more than one lobe but less than the entire lung, subsequent to a preliminary three-rib tailoring thoracoplasty in this institution. There were no deaths. Two patients incurred pneumothorax at the time of thoracoplasty because of inadvertent entrance into the pleural space. One of these required a short period of water-seal drainage.

The types of subsequent resections carried out are summarized in Table I and, as can be seen, 19 of the 31 patients were left with only basal segments following resection. In 6 patients, the fourth rib was removed in addition to the fifth rib at the time of resection, in order to obtain additional collapse.

TABLE I. TYPE OF RESECTION PERFORMED IN 31 PATIENTS WHO HAD PRERESECTION TAILORING THORACOPLASTY

Left upper lobe and superior division lower lobe	14
Right upper lobe, middle lobe, and superior division lower lobe	5
Right upper lobe and middle lobe	5
Left upper lobe and wedge of lower lobe	5
Right upper and middle lobes and wedge of lower lobe	2
	31

In addition to the larger volume of resected lung, these patients were usually left with raw segmental surfaces. They had, therefore, the two chief predisposing factors to space problems. In spite of this fact, only 2 of the patients developed this complication, an incidence of 6 per cent.

One such patient who had undergone resection of all but the basal segments of the right lower lobe retained a space even though her thoracoplasty was increased to the fifth rib at the time of resection She required tube drainage for 6 weeks before the space was obliterated The second patient who had resection of the right upper lobe and superior segment of the lower lobe retained a pleural space which would not further decrease He developed tuberculous empyema several months postoperatively Both of these complications seem attributable to the ravaged state of the lung that was left behind We are convinced that many areas of lung originally affected even though beautifully cleared by treatment are reluctant to expand much beyond their accustomed size This factor, however difficult to define or estimate is nevertheless very real

SUMMARY AND CONCLUSION

When, in the management of far advanced pulmonary tuberculosis by resection, it appears likely that only a small portion of the lung will be left behind, some degree of tailoring of the hemithorax is necessary In a series of 31 cases, we have anticipated this circumstance by careful preoperative study and have prepared for it by a preresection thoracoplasty This practice has rewarded us by an incidence of complication far below the expected The added surgery has likewise caused a low incidence of morbidity

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AN EVALUATION OF TECHNIQUES OF PULMONARY RESECTION FOR TUBERCULOSIS

David V. Pecora, M.D., Ray Brook, N. Y.

Although pulmonary resection for tuberculosis has been popular for a number of years, opinions vary among surgeons regarding various technical aspects. For instance, Steele[1] found that a considerable proportion of surgeons do not use subsegmental resection or have reservations regarding its use. Some prefer to use lobectomy in preference to smaller resections in patients harboring tubercle bacilli resistant to antituberculosis drugs. A number of writers have discussed the superiority of various types of bronchial closure. Yet, a review of the recent literature fails to yield convincing evidence to support many of the claims which have been made. In order to attempt to answer some of the more important questions which have been raised, the surgical experience at the Ray Brook State Tuberculosis Hospital between January, 1950, and January, 1957, has been reviewed.

TYPE OF RESECTION

It has been stated that the risk of pulmonary resection increases with the amount of tissue removed. Generally, this conclusion seems to be supported by the data in Tables I and II. Included in these tables are only pure procedures, combinations of different procedures at the same operation having been eliminated. Segmental resection, lobectomy, and pneumonectomy were performed by the individual ligation technique. The pleural surfaces were not routinely approximated but care was exercised to control bleeding and air leaks by suture or ligature. Subsegmental resections were performed exactly as segmental resections except that the hilar dissection occurred at the subsegmental level. Wedge resections were performed according to two general techniques, "open" and "closed." The "open" technique (Fig. 1) consisted of progressively cutting and suturing the lung with either interrupted fine silk or continuous atraumatic chromic catgut. The "closed" technique (Fig. 2) consisted of blocking off the lesion with clamps, suturing beneath the clamps, and then amputating the lesion external to the suture line. Again, either interrupted fine silk or continuous atraumatic chromic catgut in two layers were employed.

The wedge-segmental resection consisted of preliminary isolation and division of the segmental vessels and bronchi and development of the intersegmental plane until disease was encountered entering the adjacent segment, followed by

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removal of the remaining diseased tissue by either "open" or "closed" wedge technique. The "closed" type is illustrated in Fig. 3. The wedge-segmental resection has proved extremely useful in conserving functional tissue.

Before the various types of surgery can be compared, it is important to know whether or not they have been performed upon patients harboring culturable tubercle bacilli, as it has been our experience that this affects the incidence of tuberculous complications. This is evident when one compares Table I and Table II. Moreover, in searching for standards for comparison it appears appropriate to employ the postoperative complications and deaths occurring within one month following surgery. Since results were similar employing the "closed" and "open" techniques, no attempt is made to differentiate them.

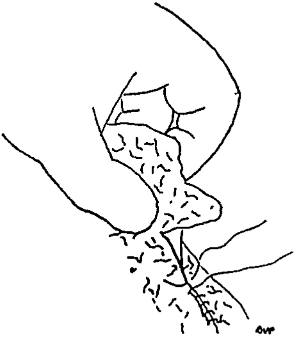

Fig 1.—"Open" wedge resection

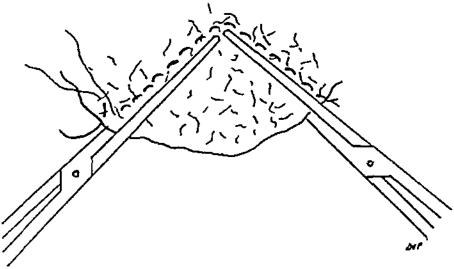

Fig. 2.—"Closed" wedge resection

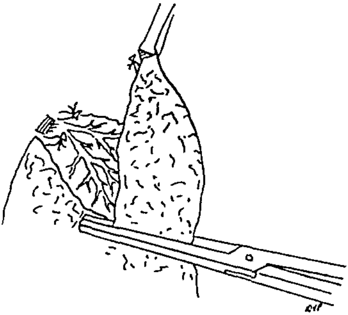

Fig 3.—"Closed" wedge-segmental resection

The incidence of postoperative hemothorax is not related to the size of the resection; this is to be expected since bleeding has usually been found to emanate

TABLE I. TYPE OF RESECTION BY EARLY POSTOPERATIVE COMPLICATIONS—PATIENTS HARBORING CULTURABLE TUBERCLE BACILLI

PROCEDURE	NUMBER	HEMO-THORAX	OPERATIVE SPREAD	BRONCHO-PLEURAL FISTULA OR EMPYEMA	OPERATIVE DEATH
Wedge	37	0	1	3	0
Wedge-segmental	17	0	0	2	0
Subsegment or segment	4	0	0	2	0
Lobectomy	26	0	1	4	0
Pneumonectomy	15	0	0	4	2
Total	99	0	2	15	2

TABLE II. TYPE OF RESECTION BY EARLY POSTOPERATIVE COMPLICATIONS—PATIENTS HARBORING NO CULTURABLE TUBERCLE BACILLI

PROCEDURE	NUMBER	HEMO-THORAX	OPERATIVE SPREAD	BRONCHO-PLEURAL FISTULA OR EMPYEMA	OPERATIVE DEATH
Wedge	178	3	0	1	1
Wedge-segmental	34	2	1	1	0
Subsegment or segment	25	1	0	0	0
Lobectomy	39	0	0	2	0
Pneumonectomy	12	0	0	1	1
Total	288	6	1	5	2

from chest wall vessels. The incidence of operative spread of disease also appears unrelated to the size of the resection. This is also to be expected since this complication appears generally related to factors such as amount of sputum, position of the patient during surgery, conduct of anesthesia, and the speed with which the bronchus leading to the source of sputum is occluded. On the other hand, the incidence of bronchopleural fistula and empyema does appear generally related to the size of resection. This can be explained to a great extent on the basis of the fact that more difficulty is experienced in obliterating the pleural space after larger resections. This is especially so in the pneumonectomy group.

The problem of obliterating residual pleural spaces following pneumonectomy has been simplified by the following practices. After resection the pleural cavity is drained with the aid of an apparatus previously described.[2] Thereafter, until thoracoplasty is performed, approximately 3 weeks later, the pleural cavity is maintained as dry as possible by thoracentesis. After thoracoplasty is performed, any remaining pleural air and fluid is aspirated before the wound is closed. If the pleural cavity contains a considerable amount of clotted exudate, a small incision is made through the bed of a resected rib and the clots removed, care being taken to prevent unnecessary bleeding. If the parietal pleura should prove too rigid to collapse firmly against the mediastinum, it is removed according to the method of Grow.[3]

Although three of the four early deaths followed pneumonectomy, it should be noted that one, a cardiac arrest during surgery, was apparently due to anesthesia difficulties. In one patient a lobectomy was planned but, because of hemorrhage due to laceration of the pulmonary artery, a pneumonectomy was performed. Although the hemorrhage was thus controlled the patient lived only

2 hours postoperatively. This death might well be credited to the lobectomy group. The third patient died 5 days postoperatively of cor pulmonale and pulmonary edema. *The fourth patient died of intrapleural hemorrhage following* wedge resection. Since bleeding appeared to emanate from the chest wall, this complication could have occurred following any type of resection.

IMPORTANCE OF EXTENT OF DISEASE

Tables III and IV summarize the early complications according to the estimated volume of surgically treated lung involved by disease. It is obvious that the incidence of bronchopleural fistula and empyema correlates even better with the extent of disease than with the type of resection performed. Indeed, this may very well be the principal determining factor in prognosis following various types of resection. It is interesting that the incidence of hemothorax did not correspond to the amount of disease, confirming the impression that this complication is due to the occasional chest wall bleeder which is accidentally overlooked. As in Tables I and II and for similar reasons there appears to be little correlation between extent of disease and incidence of operative spread of disease.

Table III *Extent of Disease in the Surgically Treated Lung by Early Postoperative* Complications—Patients Harboring Culturable Tubercle Bacilli

ESTIMATED VOLUME OF DISEASED LUNG	NUMBER	HEMOTHORAX	OPERATIVE SPREAD	BRONCHOPLEURAL FISTULA OR EMPYEMA	OPERATIVE DEATH
Less than half	74	0	2	10	0
More than half	25	0	0	5	2
Total	99	0	2	15	2

Table IV Extent of Disease in the Surgically Treated Lung by Early Postoperative Complications—Patients Harboring *No Culturable Tubercle Bacilli*

ESTIMATED VOLUME OF DISEASED LUNG	NUMBER	HEMOTHORAX	OPERATIVE SPREAD	BRONCHOPLEURAL FISTULA OR EMPYEMA	OPERATIVE DEATH
Less than half	260	6	1	4	2
More than half	28	0	0	1	0
Total	288	6	1	5	2

TREATMENT OF THE BRONCHUS

In the series of resections other than wedge resections, the proximal end of the divided bronchus was closed with end on fine silk sutures. Prior to early 1954, the bronchial stump was almost always covered with pleura or pulmonary tissue; since that time the bronchial stump has not been covered except following some pneumonectomies. Allowing for factors such as drug therapy, bacteriology, and extent of disease, it has been impossible to demonstrate a difference in incidence of bronchopleural fistula in the two groups of patients. Moreover, exploration of a number of uninfected pleural air spaces communicating with the bronchial tree has usually demonstrated these communications to lie on the lung surface and the bronchial stump to be well healed. This has been true even after obviously diseased bronchi have been divided and sutured, provided antituberculous drug therapy has been administered. Generally speaking, the occurrence of pleural empyema seems to precede rather than follow reopening of a sutured bronchus.

PRERESECTION THORACOPLASTY

Most surgeons agree that thoracoplasty may be indicated following resection to obliterate remaining pleural spaces or empyema. However, the place for preresection thoracoplasty is not well defined. Tables V and VI were compiled in an attempt to evaluate preresection thoracoplasty in the light of other important factors which affect early postoperative results. It is to be expected that the incidence of operative spread of disease and postoperative hemothorax would not be affected by preresection thoracoplasty. It is interesting that the incidence of bronchopleural fistula and empyema is higher in patients who have had preresection thoracoplasty. This difference is probably at least partially due to the fact that this group represents patients with the greater amount of disease. However, the results may to some extent indicate the difficulty one experiences in filling the conical apical pleural space which frequently exists following resection under thoracoplasty.

TABLE V. PRERESECTION THORACOPLASTY BY EARLY POSTOPERATIVE COMPLICATIONS—PATIENTS HARBORING CULTURABLE TUBERCLE BACILLI

	NUMBER	HEMOTHORAX	OPERATIVE SPREAD	BRONCHOPLEURAL FISTULA OR EMPYEMA	OPERATIVE DEATH	NUMBER WITH OVER HALF OF OPERATED LUNG DISEASED
No thoracoplasty	74	0	1	8	1	14
Thoracoplasty	25	0	1	7	1	11
Total	99	0	2	15	2	25

TABLE VI. PRERESECTION THORACOPLASTY BY EARLY POSTOPERATIVE COMPLICATIONS—PATIENTS HARBORING NO CULTURABLE TUBERCLE BACILLI

	NUMBER	HEMOTHORAX	OPERATIVE SPREAD	BRONCHOPLEURAL FISTULA OR EMPYEMA	OPERATIVE DEATH	NUMBER WITH OVER HALF OF OPERATED LUNG DISEASED
No thoracoplasty	266	6	1	4	2	18
Thoracoplasty	22	0	0	1	0	10
Total	288	6	1	5	2	28

DISCUSSION

There appears to be little reason to exclude any of the types of pulmonary resection reviewed in this communication from the armamentarium of a surgeon on the assumption that it carries too great a risk. Each technique has its applications and, if properly used, carries a low morbidity Indeed, what determines to a great extent the incidence of serious complications and mortality is the extent of disease, which fundamentally affects both the technical difficulties encountered at *operation and the physiology of the patient*

There is no evidence that lobectomy is more valuable than any other type of resection in the treatment of patients harboring resistant organisms What seems important is that the major disease be removed This may require a wedge resection or a pneumonectomy Furthermore, any type of resection without antituberculous drug protection should be avoided If one employs drugs to which the patient's tubercle bacilli are sensitive the fact that the organisms are resistant to other drugs is unimportant [4, 5]

Our results with single layer closure of the bronchus have been excellent, indicating that little is to be gained by adopting more elaborate techniques This assumption seems further supported by the fact that covering the bronchus with pleura or pulmonary tissues has not improved results Two factors of importance in the prevention of bronchopleural fistula and empyema are early obliteration of pleural air spaces and prolonged antituberculous drug therapy Bronchial disease, although emphasized by others, does not seem to predispose to the occurrence of bronchopleural fistula to an appreciable extent

There is no evidence that preresection thoracoplasty is of value On the contrary, it may predispose to poor results

SUMMARY

Seven years' experience with various types of resections for pulmonary tuberculosis is reviewed By judicious use of the procedures described, a maximum amount of functional lung tissue can be preserved The postoperative results are determined to a great extent by the amount of disease present There is no evidence that lobectomy is superior to any other procedure in the treatment of patients with resistant organisms Bronchial disease is of little importance provided adequate antituberculous drug therapy is available The simplest bronchial closure yields excellent results There is no evidence that preresection thoracoplasty *is of value*

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PULMONARY ABSCESS: A STUDY OF 70 CASES

Daniel N. Pickar, M.D., and William F. Ruoff, M.D.,** Louisville, Ky.*

PULMONARY abscess has long been recognized as one of the most serious diseases of the lungs and, prior to the availability of the antimicrobial agents, the prognosis was extremely poor, both as to morbidity and mortality.[1, 2] With the advent of the sulfonamides, penicillin, and the other antimicrobial agents, and with the development of better techniques in the field of pulmonary surgery, the prognosis for these cases has greatly improved.[3, 4]

It is the purpose of this paper to present a study of 70 consecutive cases of pulmonary abscess treated at the VA Hospital, Louisville, Ky., during the past 10 years. Abscesses resulting from tuberculosis, fungus, parasitic infection, and carcinoma constitute special categories and were purposely omitted from this study.

METHODS AND MATERIALS

All cases of pulmonary abscess in this series were referred to the Chest Therapy Board for evaluation and recommendations as to treatment. The Board consists of the Chief of the Section on Chest Diseases, the Chief of the Radiology Service, the Consultant in Chest Diseases, and the Consultant in Thoracic Surgery. The initial plan of management was to place the patient on bed rest and, after sputum specimens had been collected for culture, an antimicrobial agent was started. It was the preference of the Medical Service to start the patients on penicillin alone, usually in a dosage of 100,000 units of crystalline penicillin every 3 hours or 600,000 units of procaine penicillin twice daily. This was not a fixed policy, however, and the responsible physician could use any antibiotic, alone or in combination, which he felt desirable, particularly if the patient had received antibiotic therapy prior to admission. Subsequent antibiotic therapy was dictated by the clinical response and the results of bacteriologic determinations, including sensitivity studies. Auxiliary supportive measures which were employed as indicated were postural drainage,

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From the Medical Service, Veterans Administration Hospital, Louisville, Ky., and the Department of Medicine, University of Louisville School of Medicine.

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*Chief of the Section on Chest Diseases, VA Hospital, and Assistant Professor of Medicine, University of Louisville School of Medicine.

**Resident in Medicine, VA Hospital, Louisville, Ky.

bronchodilator drugs, expectorants, blood tranfusions, and a nutritious diet Necessary procedures for the recognition and amelioration of co existing pulmonary and systemic diseases were carried out

The response of the abscess to medical treatment determined whether or not surgical treatment was indicated In general, surgery was felt to be indicated if the abscess persisted or if carcinoma was suspected

RESULTS OF STUDY

Race, Age, and Sex —

Of the 70 patients with pulmonary abscess 59 were white and 11 were Negro There was a uniform distribution in each 10 year period from 20 to 60 years of age Only 5 7 per cent of the patients were beyond 60 years of age All patients were males

Symptoms —

The duration of symptoms prior to admission varied from one month or less up to 26 months Thirty patients (42 8 per cent) had had symptoms one month or less Fifty six patients (80 per cent) had had symptoms 5 months or less Five patients (7 2 per cent) had had no symptoms prior to admission Three of these 5 developed abscesses after admission to this hospital

Table I shows the incidence of symptoms in the 70 patients

TABLE I INCIDENCE OF SYMPTOMS

Cough	(61)	87 2%	Weakness	(9)	12 8%
Purulent sputum	(52)	74 2%	Malaise	(8)	11 4%
Chest pain	(36)	51 4%	Anorexia	(7)	10 0%
Hemoptysis	(32)	45 7%	Joint distress	(4)	5 8%
Weight loss	(25)	35 7%	Headache	(3)	4 3%
Fever	(25)	35 7%	Dyspnea	(2)	2 8%
Chills	(16)	22 9%	Abdominal pain	(2)	2 8%
Night sweats	(11)	15 8%	Stiff neck	(1)	1 4%

Pre Existing or Co Existing Disorders —

Nonpulmonary disorders Seven patients had severe oral sepsis, 5 had diabetes mellitus, 4 were chronic alcoholics 3 had neurological disease, and 2 had cerebral arterial thrombosis Fifteen patients had one each of the following disorders post tonsillectomy, thrombophlebitis, dorsal kyphosis arteriosclerotic cardiovascular disease, old chest injury, upper gastrointestinal hemorrhage of unknown cause, anxiety reaction, chronic pancreatitis, periarteritis nodosa, syphilis, lymphatic leukemia, cirrhosis, fracture, malnutrition, and coronary insufficiency

Pulmonary disorders Table II shows the incidence of pre existing or co existing pulmonary disorders

In the 2 cases of bronchial obstruction, one was due to a narrowed bronchus from an unknown cause, and the other was caused by a rupture of a calcified lymph node through the bronchial wall

Laboratory Studies —

Initial white blood count Twenty four patients (34 per cent) had a total white count of 5,000 to 10,000 per cubic millimeter In the 10 000 to 15 000

TABLE II. PULMONARY DISORDERS

Pneumonia	11
Pulmonary emphysema	6
Recurrent abscesses	3
Bronchiectasis	2
Bronchial obstruction	2
History of pneumonia and previous lung abscesses	1
Anomalous bronchi	1
Pulmonary infarct	1

range were 20 patients (28.9 per cent). In the 15,000 to 30,000 range were 25 patients (35.7 per cent). The patient with lymphatic leukemia had a total count of 495,000 white cells per cubic millimeter.

In the differential, there was a definite shift to the left with 85 per cent of the patients showing more than 60 per cent granulocytes.

Anemia: Twenty patients (28.6 per cent) had hemoglobin levels under 12 Gm., red blood cell counts under 4,000,000, and/or a hematocrit under 40 per cent.

Bacteriologic studies: Table III represents a composite in each case of one or more cultural studies for the predominating organism. Verification was also obtained in most of the surgically treated abscesses by a direct study of the resected abscess.

TABLE III. BACTERIOLOGIC STUDIES

Streptococcus	(48)	68.6%
Diplococcus pneumonia	(5)	7.1%
Friedländer's bacillus	(4)	5.7%
Hemolytic *Staph. aureus*	(3)	4.3%
Streptococcus plus Friedländer's bacillus	(2)	2.9%
Inconclusively demonstrated	(8)	11.4%
Totals	70	100.0%

Location of Abscesses.—

Table IV shows the location of the abscesses.

TABLE IV. LOCATION OF THE ABSCESS

Right upper lobe	(23)		32.9%	
Right middle lobe	(3)		4.3%	
Right lower lobe	(15)		21.4%	
Total		41		58.6%
Left upper lobe	(10)		14.3%	
Lingula	(4)		5.7%	
Left lower lobe	(10)		14.3%	
Entire left lung	(1)		1.4%	
Total		25		35.7%
Bilateral		4		5.7%
Totals		70		100.0%

Cavity Size.—

In 41 patients (58.6 per cent), the abscesses were 4 cm. or less in the greatest diameter. In 23 patients (33.0 per cent), the abscesses were 4 to 8 cm.

in the greatest diameter and, in 6 patients (8.4 per cent), the abscesses were 8 to 13 cm. in diameter.

Bronchography.—

Bronchograms were performed on 12 patients (17.4 per cent) during their hospitalization. Of these, four were normal and three showed bronchiectasis. In 2 patients, the studies aided in the delineation of the abscess. The procedure was unsatisfactory in 3 patients.

Bronchoscopic Examination.—

Forty-three patients were examined bronchoscopically. Of these, 29 were normal, 2 revealed bronchial stenosis and 12 showed edema, purulent secretions or blood from the affected bronchi.

Fever.—

The maximum temperature on the day of admission was normal in 12 patients (17.1 per cent), 99° F. to 101° F. in 41 patients (58.6 per cent), and 101° F. to 104° F. in 17 patients (24.2 per cent).

The duration of fever was 3 weeks or less in 41 patients (58.6 per cent). Twelve patients (17.1 per cent) had no fever. Four patients had a persistent temperature elevation throughout their hospitalization. Of this latter group 3 died and one left the hospital against medical advice. The remaining 13 patients had a temperature elevation which subsided 2 to 9 weeks after their hospital admission.

Cavity Closure.—

Thirty-five of the 70 patients were considered to have closed cavities within a period of 10 to 120 days. The remaining 35 cavities did not close. Of this group 24 of the patients were operated upon, 5 died, 4 left the hospital against medical advice, and 2 were discharged from the hospital because they wished to continue therapy under their private physician.

Medical Therapy.—

Forty-four patients were treated medically. As soon as the abscess was diagnosed, sputum was submitted to the laboratory for smear and culture for predominating organisms and sensitivity determinations. An antibiotic was commenced immediately without awaiting the results of the above studies. The choice of an initial antibiotic varied and the selection was influenced by the preference of the ward physician and the consultant staff. In 21 patients, penicillin was used alone; in 12, penicillin plus a tetracycline drug was administered; in 3 patients, penicillin plus streptomycin was used; and in one patient a tetracycline drug alone was used. In another single instance, because of the consideration of possible tuberculosis, streptomycin plus isonicotinic acid hydrazide was given.

It was in the patients with Friedlander's and staphylococcus infections that the sensitivity studies proved to be most helpful in the choice of an effective antibiotic. There were 4 such patients in whom penicillin and/or a tetracycline drug was initially used, and later a tetracycline drug plus chloromycetin or chloromycetin alone was used.

It is interesting that 3 patients effected a complete recovery without any antibiotic therapy. Of these, 2 had abscesses which closed during a brief observation period and the other refused any antibiotic therapy.

Cause of death in 5 patients treated medically: Patient G. J. E., a 45-year-old white man, died 7 days after admission. He had a severe Laennec's cirrhosis in addition to his pulmonary abscess.

Patient E. E. E., a 36-year-old white man, was admitted to the hospital with periarteritis nodosa. His death resulted from a terminal Friedländer's pneumonia and multiple Friedländer's abscesses in the lung 17 months after admission.

Patient S. R., a 56-year-old white man, was hospitalized for pulmonary abscess for 42 days. Terminally, he had a bronchopneumonia.

Patient F. L., a 72-year-old white man, had completely recovered from his pulmonary abscess, but died from an acute coronary occlusion when he was being discharged from the hospital.

Patient B. W., a 43-year-old white man, had fully recovered from multiple Friedländer's abscesses treated 10 months previously. On his readmission, he again had Friedländer's pneumonia and abscesses. He had had diabetes mellitus for many years. On his final admission, he had a Friedländer's septicemia and a severe jaundice, the cause of which was not determined. He died 15 days after this second admission.

Surgical Therapy.—

It was our policy that medical therapy be given to the patient with an uncomplicated case to the point where no further improvement was considered probable. When carcinoma was suspected, or when surgical complications existed, surgery was advised earlier. Table V shows the reasons for surgery in the 26 cases in which surgery was performed.

TABLE V. REASONS FOR SURGERY

Persistence of abscess and infiltrate on medical therapy	18
Suspected carcinoma	5
Bronchiectasis	1
Abscess rupture through the diaphragm	1
Continuation of open thoracotomy instituted in another hospital	1
Total	26

In reviewing the patients who had an operation, 19 (73 per cent) had had less than 5 weeks of medical therapy. We are of the opinion, after review of the cases individually and applying our present-day criteria for surgical consideration, that 8 of these patients would now be given a longer trial at medical therapy prior to surgery.

Type of surgery performed: The type of surgery performed is shown on Table VI.

Causes of death in surgically treated patients: Patient P. O., a 56-year-old man, had a segmental resection of the RUL and RML and had repeated complications, including empyema and bronchocutaneous fistula, following the initial surgery. Many subsequent surgical procedures were performed. He died 17 months after the initial surgery from pulmonary hemorrhage.

TABLE VI. TYPE OF SURGERY PERFORMED

Right Lung		
Right pneumonectomy	2	
RUL lobectomy	4	
RUL and RML lobectomies	2	
RLL lobectomy	3	
RUL lobectomy and additional segmentectomies	1	
Multiple segmentectomy of one or two lobes	3	
Total		15
Left Lung		
Left pneumonectomy	2	
LUL lobectomy	2	
LLL lobectomy	1	
LUL lobectomy and segment LLL	1	
LUL wedge resection	1	
LUL and LLL wedge and segmentectomy	1	
LLL segmentectomy	1	
Total		9
Thoracoabdominal exploration		1
Open thoracotomy		1
		26

Patient S. H., a 60-year-old man, had chronic lymphatic leukemia which was the major factor in his death 5½ months after admission. He had had an open thoracotomy for a persistent abscess.

Patient R. B., a 29-year-old man, had a left pneumonectomy and died 3 hours postoperatively from shock and acute pulmonary edema.

Patient G. J. B., a 36-year-old man, was admitted with a pulmonary abscess which had ruptured through the diaphragm. This required immediate exploration. He died 84 days after admission from a brain abscess, peritonitis, and generalized sepsis.

Patient P. C., a 40-year-old man, had a right pneumonectomy and died from cardiac standstill during surgery.

Patient M. H. J., a 28-year-old man, had a right pneumonectomy and died 3 hours postoperatively from acute pulmonary edema.

Patient C. J. A., a 43-year-old man, had a right upper lobe and a right middle lobe lobectomy and died 22 days postoperatively from persistent sepsis and acute degeneration of the liver.

Duration of Hospitalization.—

TABLE VII. DURATION OF HOSPITALIZATION

	SURGICAL	MEDICAL
1 month or less	1	7
1-2 months	3	13
2-3 months	5	12
3-4 months	7	8
4-5 months	4	3
5-6 months	3	0
6-7 months	0	0
7-8 months	1	1
Longer than 8 months	2	0
Totals	26	44

Total Duration of Morbidity.—

In determining the duration of morbidity we have included the period of time from the onset of the first distressing symptom to the date of admission to the hospital, the period of hospitalization, and the post-discharge period that was required for additional convalescence up to the time the patient was able to return to work.

The following Table VIII shows the total duration of morbidity.

TABLE VIII. DURATION OF MORBIDITY

	SURGICAL	MEDICAL
1 month or less	0	2
1-2 months	0	5
2-3 months	1	10
3-4 months	6	10
4-5 months	2	9
5-6 months	5	1
6-7 months	5	1
7-8 months	1	1
8-9 months	2	3
9-10 months	1	2
10 months or more	3	0
Totals	26	44

In general, the surgically treated patients had a longer period of morbidity than did the medically treated group. In this connection, it should be recalled that patients requiring surgery were, as a group, more seriously afflicted and, in most cases had had a course of medical therapy which had proved inadequate.

DISCUSSION

The proper use of antibiotics is essential to the effective management of pulmonary abscess. Our studies emphasize the need for identification of the offending organism at the onset of therapy and the need for subsequent studies of the sputum, preferably at weekly intervals, to detect the development of bacterial strains that are resistant to the antibiotic being employed. In our series, there were 4 patients whose original cultures grew Friedländer's bacilli. These organisms were not sensitive to penicillin. There were 2 patients in whom the initial cultures revealed both a streptococcus and Friedländer's bacilli and, with subsequent cultures, sensitivity determinations and clinical correlation, the Friedländer's bacillus was felt to be the offending organism. In 3 patients, hemolytic *Staphylococcus aureus* was not isolated initially but was subsequently cultured. This organism was resistant to penicillin. In all of the above cases, the employment of an antibiotic to which the organism was sensitive was of vital importance.

The selection of patients for surgery is an individual problem. We consider the indication for surgery to be the conclusive demonstration that medical therapy has failed. During the past few years, we have applied this criterion more vigorously than we did during the first part of the study. Our studies reveal that in some patients we performed operation after a brief period of medical therapy and in others while they were still showing some improvement.

We now believe that medical therapy of only 1 to 2 weeks is inadequate, and that if any degree of improvement can be demonstrated medical therapy should be continued In addition, we believe that operation should be performed if the presence of carcinoma is suspected or it there exist or develop complications which are considered to be surgical such as rupture of the abscess empyema, bronchiectasis, or bronchostenosis

It is to be noted that 3 of the 4 patients who had a pneumonectomy died during surgery or in the immediate postoperative period It has been stressed by other workers[4] [5] that this procedure for pulmonary abscess carries with it a high incidence of complications and a high mortality rate

The use of antibiotics and the development of better anesthesia and surgical techniques have substantially improved the prognosis in pulmonary abscess However, it still remains a serious problem In our series, approximately 70 per cent of the patients required hospitalization of from 1 to 4 months In 20 per cent, it exceeded 5 months In 17 1 per cent the disease terminated in death Thus, in spite of medical progress, pulmonary abscess continues to be a prolonged morbid process with a substantial mortality rate

SUMMARY AND CONCLUSIONS

Seventy cases of pulmonary abscess treated at the VA Hospital, Louisville, Ky , have been reviewed Forty four of these were treated medically and 26 surgically There were 12 deaths, representing a mortality of 17 1 per cent

We consider pulmonary abscess to be primarily a medical problem Surgery should be performed, however, if continued radiologic and clinical improvement under medical therapy cannot be demonstrated, if carcinoma is suspected, or if complications exist or develop which are considered surgical

Cultures of the sputum, including sensitivity studies of the organisms, should be made immediately These studies should be repeated at weekly intervals in order to be certain of the antibiotic sensitivity of the offending organism This is particularly true in cases in which the infection is caused by *Staphylococcus aureus* or Friedlander's bacilli

Although the prognosis in pulmonary abscess has improved with the advent of antibiotics and the development of improved anesthesia and surgical techniques, it continues to be a prolonged morbid process with a substantial mortality rate

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ANOMALOUS SPLITTING OF THE UPPER LOBE BRONCHUS IN RIGHT AND LEFT LUNGS: WITH A NOTE ON THE INCIDENCE IN THE LONDON AREA OF LEFT MEDIAL BASAL SEGMENTS*

E. A. Boyden, Ph.D. (Med.Sc.), Seattle, Wash., and
D. H. Tompsett, Ph.D., London, England

IN THE MUSEUM of the Royal College of Surgeons in London there are some twenty preparations of human lungs in which the whole tracheobronchial tree (and frequently the pulmonary vessels) have been injected by the superb Marco resin technique devised by Dr. D. H. Tompsett.[10] Because of the number and perfection of these casts of distended lungs, the collection provides an unusual opportunity to study variations in the patterns of the bronchopulmonary segments.

Recently, while in residence at the College, the senior author took time to make such a study and found, to his surprise, four pairs of lungs in which there were two upper lobe stems originating from either the right or left main bronchus—two on the left side and two on the right. These had been noted by Dr. Tompsett but not hitherto described. Moreover, the few cases which have appeared in the literature have been based largely on bronchograms. For these reasons, it has seemed desirable to place these cases on record.

CASTS OF RIGHT UPPER LOBE

Figs. 1 and 2 are sketches of the segmental bronchi of two right lungs. That of Fig. 1 shows two upper lobe stems arising in close proximity and having a combined area of origin 1.6 cm. in length. The second sketch (Fig. 2), drawn from the posterior side, shows two upper lobe stems which are further apart. The length of the combined area of origin in this cast is 2.4 cm. In each case the higher of the two bronchi supplies the zone of the right apical segment; the lower one the territories of the anterior and posterior segments. Foster-Carter,[6] in his Fig. 20A, reproduces a bronchogram which seems to resemble closely the specimen shown in our Fig. 2. Incidentally, Fig. 2 displays another anomaly—namely, dual origin of the branches of the superior (subapical) segment (Boyden,[2] Fig. 72).

From the Departments of Anatomy, University of Washington, Seattle, Wash., and Royal College of Surgeons of England, London, England.

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A somewhat different pattern has been published by Brock[3] who injected the upper of two upper lobe bronchi in an anatomical specimen. In this case, the two bronchi had approximately the same position as those in Fig. 2 (his Fig. 128), but the upper one was distributed to only the mediastinal portion of *the apex and not to the whole of the zone comprising the apical segment—an* area corresponding to that supplied by the first branch of the left main bronchus in Fig. 4.

From specimens of this kind, it is but a short step to rarer cases in which a ramus of the upper lobe originates at the junction of the trachea and the right upper lobe bronchus (cf. Boyden,[2] Fig 31) and even to rami which are frankly tracheal in origin. One of the most interesting of these is being prepared for publication by Dr. David Browne[4] of Charing Cross Hospital, London.

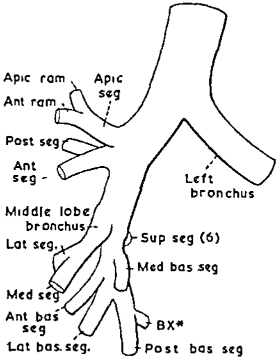


Fig 1

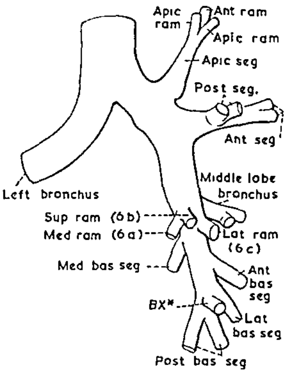


Fig 2

Fig. 1—Anterior view of right bronchial tree of Cast *M1001* in Royal College of Surgeons which illustrates first stage in cleavage of the right upper lobe bronchus

Fig. 2—Posterior view of right bronchial tree of Cast *M1005* which shows separation of two components of right upper lobe bronchus Both Figs 1 and 2 are from lungs of adults

This cast has two upper lobe stems, one at the usual site (an inch above the middle lobe bronchus) and the other originating from the right lateral side of the lower trachea, almost an inch above the bifurcation. This lobe is cleft by the azygos vein.

CASTS OF LEFT UPPER LOBE

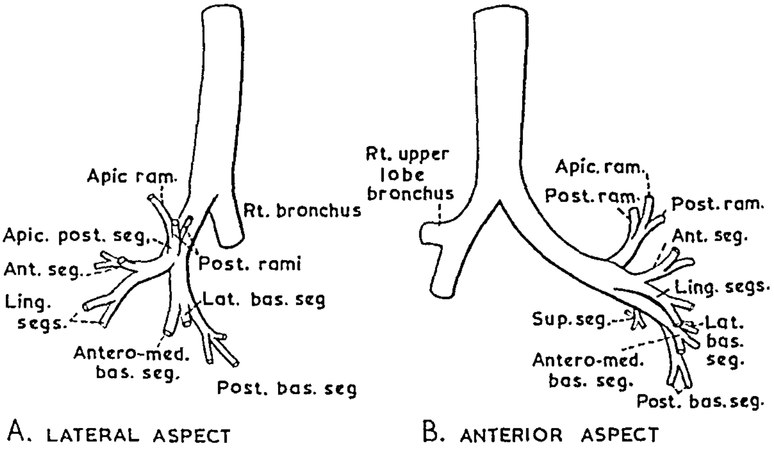
The 2 cases presented here resemble those of the right side in having the two upper lobe bronchi closely adjacent to each other. In the first one (Fig. 3), the higher of the two bronchi supplies the apical-posterior segment. The lower of the two divides almost immediately into a bronchus which supplies the anterior and lingular segments and into a lower lobe bronchus. In the book by Huizinga and Smelt[7] (their Fig. 20), there is a bronchogram of an adult patient that closely resembles that from the 15-day-old infant sh[illegible] Fig. 3.

In the second case (Fig. 4), the left main bronchus, at the usual site of bifurcation, gives rise first to a small split-off portion of the apical bronchus, then divides immediately into upper and lower lobe bronchi. Apparently, such a "splinter" bronchus is much less common on the left than on the right main bronchus.

These 2 cases are to be distinguished from a left eparterial bronchus which originates much higher up on the main bronchus. (For description of 5 such cases, see Boyden,[2] p. 217.)

THE INCIDENCE OF SEPARATE LEFT MEDIAL BASAL BRONCHI

One of the striking variations in the bronchial tree of the left lower lobe is the separate origin of the medial basal bronchus (see pink-colored bronchus, Fig. 4). Because of this aberration, the left medial basal segment was recognized as such at the last International Congress of Anatomists in Paris, 1955; and for this and other reasons (Boyden,[2] p. 30), it is believed that the so-called anterobasal segment of the London Congress of 1949 should at least be designated by the name anteromedial basal segment, as originally proposed by Jackson and Huber[8] in 1943.



A. LATERAL ASPECT B. ANTERIOR ASPECT

Fig. 3.—Drawings of left bronchial tree of Cast *S.254 1* from an infant 15 days old. Note separation of left upper lobe into apical-posterior and anterior-lingular components, with the former as the first branch of the left main bronchus.

This medial basal segment was first described by Dévé[5] in 1900. In 1949, Berg, Boyden, and Smith[1] reported its separate occurrence in 10 per cent of 60 lungs of people that had been residents of Minnesota. Four years later, Pitel and Boyden[9] reported it as occurring in 4 per cent of an additional 50 lungs from the same locality. The incidence in 110 individuals was thus 7.3 per cent. Strangely enough, 7 cases of this occur in the 21 injected specimens prepared up to this time by Dr. Tompsett at the Royal College. Subsequently, it was ascertained that Dr. David Browne[4] at Charing Cross Hospital has the same number of cases in approximately the same number of injected specimens. Therefore, the incidence of a displaced left medial basal bronchus in two London

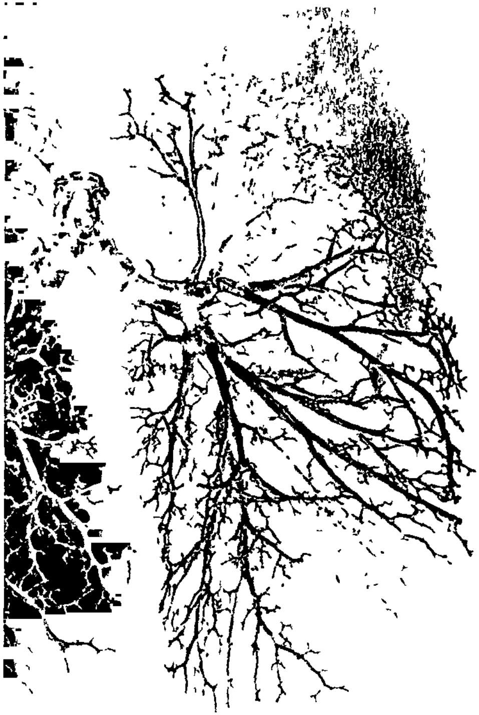


Fig 4.—Color photograph of left bronchial tree of Cast *M1003* in Royal College of Surgeons. Note first (uncolored) branch of left main bronchus, representing separately arising mediastinal ramus of apical-posterior bronchus (elements of *B^1a* and *B^1b*).

Upper lobe bronchi: *red*, larger portion of apical-posterior stem (Boyden's $B^1 + {}^2a$); *dark blue*, rest of stem (Boyden's B^2b); *dark green* (barely visible in color reproduction), anterior bronchus (Boyden's B^3); *gray*, superior lingular bronchus (B^4); *pink*, inferior lingular bronchus (B^5).

Lower lobe bronchi *yellow*, superior (apical) bronchus (B^6); *pink*, medial basal (B^7); *blue*, anterior basal (B^8), *red*, lateral basal (B^9); *green*, posterior basal (B^{10}) For reproduction of the whole tree of this specimen see Fig. 38, Tompsett.[10]

ENDOMETRIOSIS INVOLVING THE PLEURA

Charles B. Ripstein, M.D., Michael Rohman, M.D., and Jacques B. Wallach, M.D., New York, N. Y.*

INTRODUCTION

INVOLVEMENT of the pleura by endometriosis is rare, 2 cases having been reported in the literature. The following report illustrates the diagnostic and therapeutic problems encountered in this lesion.

CASE REPORT

J. W., a 24-year-old Negro nulliparous housewife, was admitted to the Bronx Municipal Hospital Center on Oct. 11, 1957, for diagnosis and treatment of a right pleural effusion. Six months prior to admission a dull right-sided chest discomfort was noted which gradually increased in intensity to a sharp "sticking" pain of severe degree, aggravated by coughing and deep respirations. Five months prior to admission, a cough developed and persisted, productive of ¼ to ½ cup of white sputum daily. A recurrent feverish sensation was noted in the afternoons. During this period, there was a fifteen pound weight loss associated with anorexia, general malaise, and easy fatigability. There had been no previous known contact with tuberculosis. Hemoptysis, wheezing, chest trauma, and foul sputum were denied. X-ray studies revealed a right pleural effusion and the patient was admitted with the diagnosis of suspected pulmonary tuberculosis.

Menarche had occurred at 14 years of age with menses appearing every 28 days and lasting from 4 to 7 days. In recent years, the amount of bleeding had increased and the early part of the menses was accompanied by moderate abdominal pain. The patient had married 4 years previously. Although no contraceptives were employed, conception had not occurred.

Physical examination revealed a well-developed and well-nourished Negro female, appearing chronically ill, with mild exertional dyspnea. Temperature was 100.6° F., pulse rate 82 per minute, respiration 28 per minute, blood pressure 110/70 mm. Hg. The positive findings were limited to the chest and pelvis. There was a definite respiratory lag with decreased expansion of the right hemithorax. The left lung was clear to percussion and auscultation, except for a few basilar rhonchi which cleared on coughing. On the right side, there were decreased-to-absent breath sounds over the lower three fourths of the chest posteriorly, dullness to percussion over this area, and fine râles above the level of dullness. Pelvic examination revealed a marital introitus and irregularity of the posterior vaginal wall with slight guarding and deep tenderness in the para-uterine area. Except for mild anemia (hemoglobin 11.0 grams per cent), the laboratory studies on this and subsequent admissions were within

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From the Departments of Thoracic Surgery and Pathology, The Bronx Municipal Hospital Center, The Albert Einstein College of Medicine, New York, N. Y.

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*Fellow of the American Trudeau Society, Medical Section of the National Tuberculosis Association.

normal limits. Repeated sputum examinations for acid fast bacilli were negative on smear and culture. Tuberculin skin testing with OT 1 10,000 and 1·1,000 was slightly positive Skin tests for histoplasmosis and coccidiomycosis were negative

On the day of admission, 1,400 c c of thin, bloody, nonclotting fluid was removed from the right pleural cavity. The fluid had a total protein of 6 5 mg per cent, 590,000 red cells per cubic millimeter, and a hemoglobin of 2 4 grams per cent Cultures from this, as well as from all subsequent thoracenteses, were negative for pathogens, including acid fast bacilli No malignant cells were seen on cytologic examination Needle biopsy of the pleura was negative for tumor or tubercles

X ray studies, which on admission revealed an extensive right sided pleural effusion and moderate displacement of the heart to the left (Fig 1), showed no evidence of underlying parenchymal disease following thoracentesis

The removal of the pleural fluid afforded relief of exertional dyspnea, but this recurred as the fluid rapidly reaccumulated and 11 days later repeated thoracentesis yielded 900 c c of similar fluid The redevelopment of hemorrhagic pleural effusion throughout the 10 months of observation at this institution was a serious problem necessitating a total of five *thoracenteses The accumulation of fluid and concomitant chest pain could not be related* to the menstrual cycle.

Tomographic and fluoroscopic studies demonstrated poor delineation and irregularity of the right diaphragm with diminished excursions, suggesting the possibility of neoplasm of the diaphragm or pleura in this region A diagnostic pneumoperitoneum was induced and radiographic studies demonstrated thickening of the right diaphragm with irregularity and scalloping (Fig 2) Films taken the next day demonstrated a right hydropneumothorax and partial collapse of the right lung (Fig 3). The passage of air from the peritoneal cavity to the right pleural space was of considerable interest as it demonstrated the presence *of a definite communication between these sites There was no evidence of such a communica*tion with the left pleural space

In view of the failure to obtain a definitive diagnosis, an open right thoracotomy was performed on Nov. 8, 1957 Two small cystic structures were loosely attached to the parietal pleura, one at the level of the fifth rib posteriorly, and the second on the dome of the dia*phragm. One of the cysts was opened and contained a small amount of chocolate colored* material There were numerous yellow pink, slightly raised and irregular plaques on the parietal pleura, and these became most numerous and confluent over the surface of the diaphragm The visceral pleura was unremarkable The diaphragm was opened and no disease was demonstrated in the muscular portion or on the inferior surface The liver and *gall bladder were negative Abdominal masses could not be palpated and there was no* fluid in the peritoneal cavity Both cysts were removed with an attached portion of parietal pleura Postoperatively, a small amount of fluid reaccumulated in the chest, but this stabilized and the patient was discharged on Dec 11, 1957, upon her own request

The gross specimen consisted of two oval cystic structures which measured 1 5 and 2.3 cm in greatest diameter The external aspect of each was smooth and gray white, with a resilient, gray white wall 1 to 2 mm in thickness. The inner lining of each cyst was smooth and shiny and the lumina contained bloody serous fluid One of the structures was attached to a flattened portion of smooth, gray white pleura which averaged 2 mm in thickness and measured 2 cm in greatest dimension. The microscopic diagnosis was "cysts lined by dense fibrous tissue showing frequent hemosiderin laden phagocytes, suggesting organizing hemorrhage The possibility of endometriosis cannot be ruled out" (Figs 4 and 5).

The patient was readmitted on March 31, 1958, when progressively severe exertional dyspnea was noted and x ray studies revealed further increase of the right pleural effusion Thoracentesis yielded 1,200 c c of thin, bloody, nonclotting fluid

Because of the diagnosis of possible endometriosis of the pleura, gynecologic consultation was obtained. The uterus was slightly enlarged, irregular, and in almost third degree retroversion. A 3 by 3 cm nodule projected from the right side of the uterus and a firm

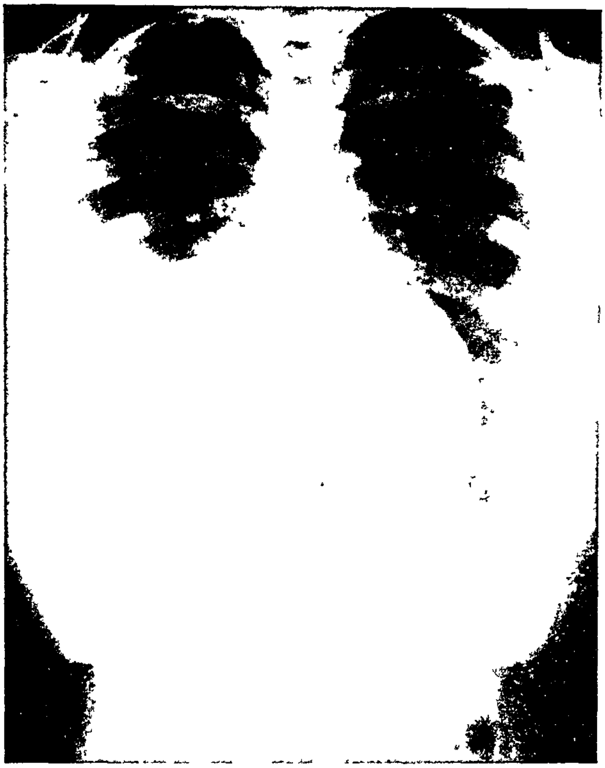


Fig 1.—Roentgenogram at the time of admission showing right pleural effusion.

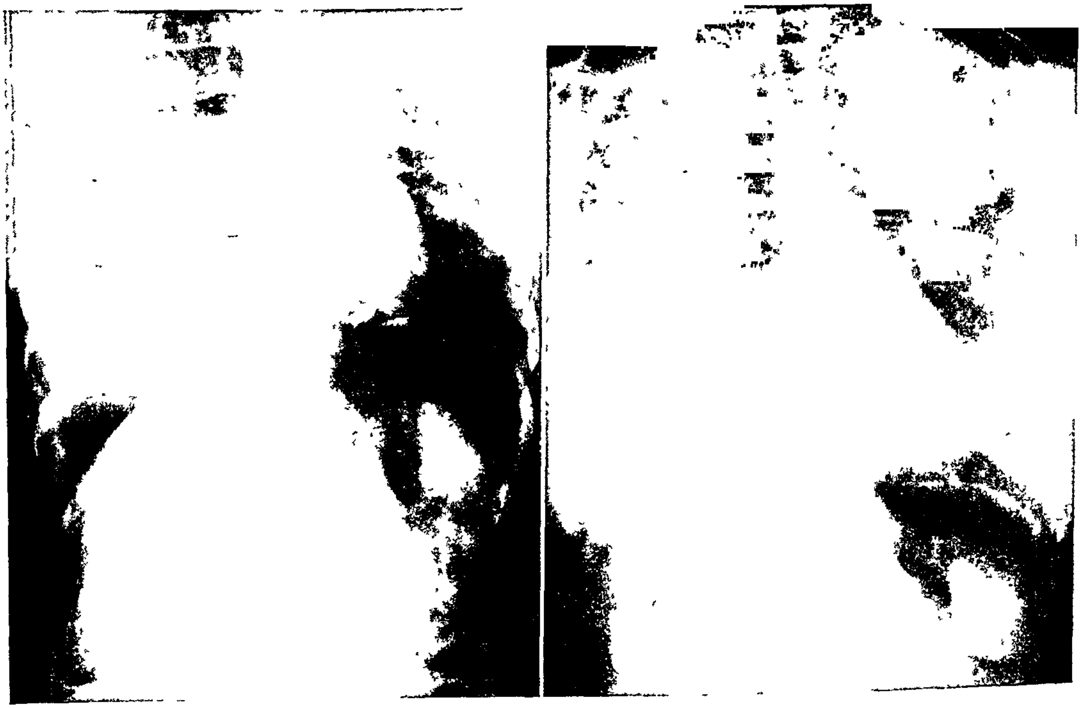


Fig. 2. Fig. 3.

Fig. 2.—Roentgenogram following pneumoperitoneum showing irregular thickening and scalloping of the diaphragm.

Fig. 3.—Roentgenogram after institution of the pneumoperitoneum showing the hydropneumothorax.

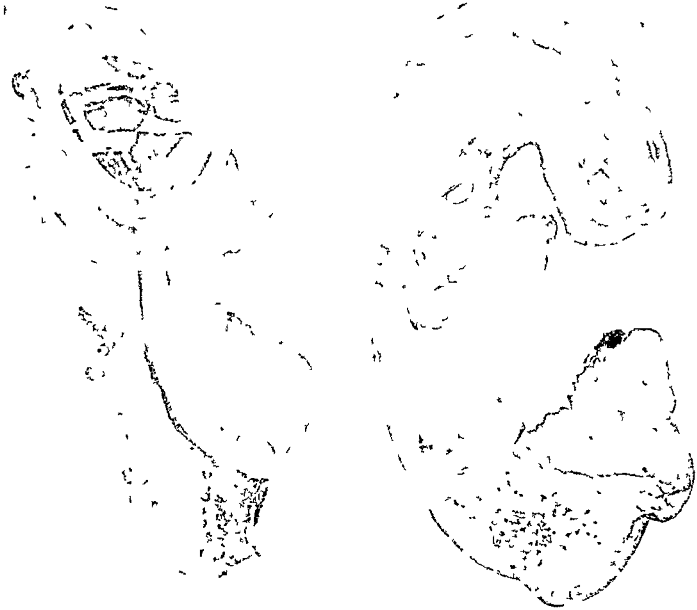


Fig 4—Biopsy of pleura and attached cysts with contained blood (Hematoxylin and eosin ×7, reduced 1/10)

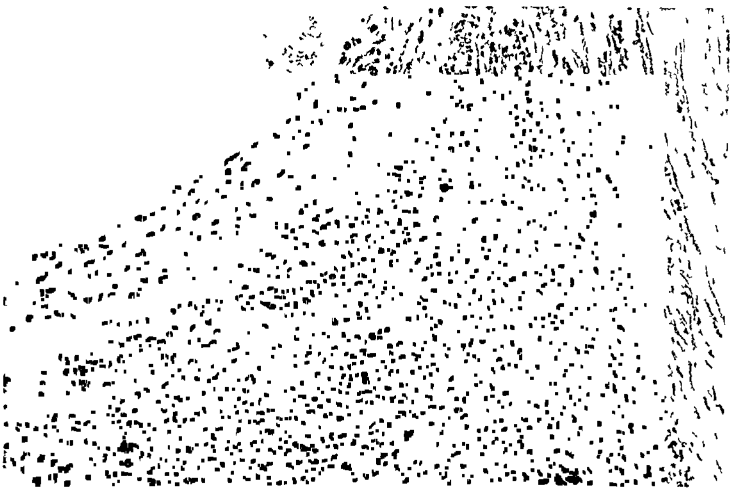


Fig 5—Higher magnification of Fig 4 showing fibrous wall ar stroma containing abundant pigment laden macrophages and few epit etrium (Hematoxylin and eosin ×250 reduced 1/5)

6 by 4 cm. nodule was palpated on the left, apparently in the broad ligament. There was nodularity and tenderness in the cul-de-sac. A hysterogram demonstrated a filling defect in the posterior wall of the uterus; the fallopian tubes appeared normal. Culdoscopy was incomplete due to obliteration of the cul-de-sac.

The patient was discharged on May 15, 1958, and readmitted for the third time on June 1, 1958, for exploratory laparotomy. On the next day, 815 c.c. of thin, hemorrhagic fluid was removed from the right pleural space. Uterine curettage and biopsy of the posterior vaginal wall revealed late secretory endometrium without tubercles and chronic inflammation of the vaginal wall. Pleural fluid reaccumulated rapidly, and 8 days after the previous thoracentesis 900 c.c. of thin bloody fluid was removed. On the following day, exploratory laparotomy revealed fallopian tubes that were patent but adherent to the posterior aspect of the ovaries. The ovaries were adherent to the region of the cul-de-sac, which was obliterated by marked inflammatory reaction. There were 100 to 150 c.c. of brownish fluid within the pelvic cavity. A 3 by 3 mm. bluish nodule, suggesting endometriosis, was adherent to the appendix. Biopsies were taken of scattered plaques of hemorrhagic tissue on the surface of the tubes and ovaries. A 2 by 2 cm. bluish cystic structure was removed from the omentum. Histologic examination of these biopsies demonstrated endometriosis (Fig. 6). Surgical sterilization was not performed.

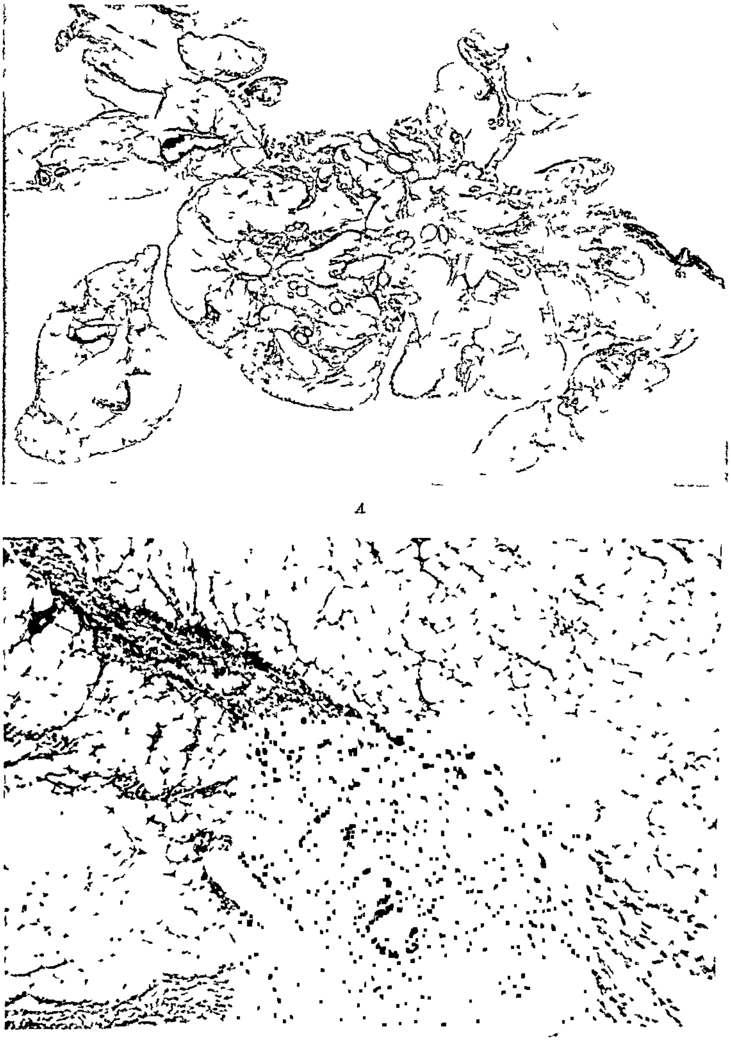
A trial of Enovid therapy (17 alpha-ethynyl-17-hydroxy-5 [10]-estren-3-one with ethynyl estradiol 3-methyl ether), 10 mg. per day, was instituted in an effort to obtain suppression of ovarian function and to prevent the reaccumulation of pleural fluid. Since discharge from the hospital on June 21, 1958, the pleural effusion has not reappeared and the patient is being followed in the outpatient department.

DISCUSSION

Two histologically proved cases of endometriosis involving the pleura have been reported previously. Brews[1] mentioned a 39-year-old woman, with ascites and right pleural effusion, who had diffuse abdominal endometriosis, involvement of the right diaphragm, and a small communication between the peritoneal and right pleural cavities. The patient was well for 3½ years following irradiation of the ovaries. Pleural involvement by endometriosis is not documented.

Barnes[2] and Nicholson[3] separately presented the same case of a 25-year-old married nulliparous woman who had recurrent hemorrhagic pleural effusion. At thoracotomy, a yellow "pellicle" was stripped from the right lung and microscopic sections showed typical endometrial tissue. A 200 mg. pellet of testosterone was implanted subcutaneously and she was advised to become pregnant. She apparently was unable to conceive and subsequently had recurrent pleural effusion. Oophorectomy was ultimately performed and endometriosis of the pelvic peritoneum was found.

Lattes and associates,[4] while presenting a case of endometriosis of the lung, referred to a report by Büngeler and Silveira[5] of a 42-year-old woman who died of "chronic pneumonia." Both pleural cavities were obliterated and there was histologic evidence of endometriosis in three small nodular masses on the right upper pleural surface. Büngeler and Silveira[5] attributed the pleural endometriosis to metaplasia or heteroplasia of the pleural mesothelium. According to this theory, peritoneal endometriosis is derived from metaplasia of the peritoneum. Since both mesothelial spaces arise from a common anlage, the embryonic coelomic cavity, it seemed reasonable that pleural endometriosis might similarly be the result of metaplasia.



A

B

Fig 6 —*A*, Section of omentum containing endometrium (He
reduced 1/10) *B*, Higher magnification of omentum showing well d
and stroma in fat tissue (Hematoxylin and eosin ×115, reduce

Lattes[4] described a 34-year-old woman with hemoptysis associated with menstruation of 3 years' duration. Roentgenograms of the lungs showed a coin lesion and the resected specimen contained endometrium with decidual reaction of the stroma; pleural involvement was not mentioned. The patient apparently was cured by pulmonary resection. The authors believed that the lesion resulted from hematogenous spread and implantation of endometrium during a previous cesarean section and uterine curettage.

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The presence of a communication between the pleural and peritoneal cavities, demonstrated by the prompt development of a right pneumothorax following diagnostic pneumoperitoneum in this case, is of considerable interest. Sampson's theory that pelvic and abdominal endometriosis results from the retrograde expulsion of endometrium into these areas through the fallopian tubes may be applicable in this case. Extension into the thorax is made possible by the presence of a communication through the diaphragm.

SUMMARY

A case of endometriosis involving the pleura is reported. The patient had recurrent hemorrhagic pleural effusion, increased menses associated with moderate abdominal pain, and inability to conceive. The diagnosis was considered clinically and confirmed by histologic examination of tissue from the pleural and peritoneal cavities. Diagnostic pneumoperitoneum was followed promptly by pneumothorax, indicating the presence of a communication between the right pleural and peritoneal space, and permits the application of the implantation theory in explanation of this unusual site of endometriosis.

Two documented cases of pleural endometriosis and one of endometriosis of the lung are cited.

This pathologic process should be considered in a young woman with recurrent hemorrhagic pleural effusion of obscure etiology. Early treatment, directed at suppression of ovarian function, will provide relief of the debilitating symptoms secondary to the continuing accumulation of the irritating bloody fluid in the pleural space.

We are indebted to Mr. Milton Kurtz who is responsible for the illustrations used in this paper.

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falls vertically in an oxygen atmosphere, the surface tension on the falling surface at the gas blood interface holds the surface red cells rather rigidly in position so that there is little, if any, mixing of the surface with cells deeper in the falling film. So, no matter how long the vertical fall of the film, the surface cells become saturated quite early in the fall while the deep cells receive essentially no contact with oxygen. *Of course, if the falling film can be made turbulent,* with complete mixing into the surface film during its fall, the oxygen uptake should be enormously increased. There is some evidence that a screen surface produces enough turbulence to produce some mixing but the data of Gaertner and Kay[13] seem to show that mixing on a screen is not complete, because oxygen uptake over the first part of a fall greatly exceeded the uptake over the last part at all given flow rates.

However, turbulence from a rough surface is not the only way to mix surface and deep blood in a filming system. There are probably many ways, but one which we have found rather satisfactory in practice is to produce rapid changes in the thickness of the film and let the blood run down in rather thick waves, one wave following the other. A smooth plastic surface on which a blood film is produced by a slowly moving oscillating jet allows blood oxygenation with approximately the same efficiency as a screen surface. We have, therefore, been able to produce a filming system in which blood is laid down on a disposable vinyl surface by a moving low pressure jet. This basic system appears to us to retain the desirable features of other filming systems, and to have the great advantage that it can be essentially prefabricated and then disposed of after use.

DESCRIPTION OF APPARATUS

The Oxygenating Unit.—Oxygenation is accomplished by a blood film spread on the inside of a series of partly inflated polyvinyl bags, each 76 cm long and 40 cm wide. The bags are constructed of a specially prepared polyvinyl sheeting which is extremely hydrophobic and is essentially free of soluble plasticizer.* The bags are inserted into a Lucite retaining frame and then inflated against the frame with oxygen containing 6 per cent carbon dioxide.

Blood is introduced into the top of each bag through a silicone treated glass manifold ending in a Y shaped distributing tube for each bag. The distributing Y tubes oscillate or rock back and forth inside the bags and spread the blood into an even film on the inside of the bag at the top. The apparatus is shown diagrammatically in Figs. 1 and 2.

The bottom of each bag acts as a blood reservoir and drains into a common collecting manifold. Blood is continuously withdrawn from the collecting manifold and pumped back to the distributing tubes at the top of each bag, to maintain the film. There is no bubbling or foaming and so no antifoam is used.

The Pumps and Catheters.—The pumps are the Gibbon type consisting of several parallel tubes pressed by a revolving pair of rollers. It is, therefore, several parallel pumps, depending on the number of tubes pressed by the same

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*Manufactured by Cutter Laboratories, Fourth and Parker Streets, Berkeley, Calif.

A DISPOSABLE FILMING PUMP-OXYGENATOR

Experimental and Clinical Use in 70 Patients

John J. Osborn, M.D., Frank Gerbode, M.D., Herbert Perkins, M.D., Mark Braimbridge, F.R.C.S., Denis Melrose, M.B., and Paul Kahn, A.B., B.S., San Francisco and Berkeley, Calif.

ARTIFICIAL lungs or oxygenators usually form their blood-gas exchange surface in one of three ways: (1) by bubbling gas through blood,[1-3] (2) by filming blood over a large surface area,[4-7] or (3) by spreading blood between two thin diffusion membranes.[9] Of these methods, the bubbling method is by far the simplest but many workers have found filming methods (usually using stationary screens or rotating disks) more satisfactory. The membrane oxygenators in turn may well be superior to filming systems but they have particular problems of their own in manufacture. Design of an oxygenator, like the design of an airplane, requires that the designer list his desires in some order of priority and then reach a difficult compromise between extremes.

We have previously described a filming oxygenator which handled blood with very low measurable damage.[10, 11] For this reason and because experimental results were excellent, we have felt that it has been worth while to sacrifice some of the fine simplicity of the bubble-oxygenator for the apparently better results of a filming system.

In the requirements for a practical blood oxygenator, cleanliness and disposability rank very high. It is essential to a successful perfusion that all surfaces which the blood touches be pyrogen-free and scrupulously clean. We have, therefore, evolved a filming oxygenator in which the filming surface is of vinyl plastic film, so that the ''artificial lungs'' can be supplied sterile and ready to use and then be thrown away after use.

It has been shown that in stationary filming systems, a smooth filming surface is less efficient than a "rough" surface in allowing oxygen uptake. Gibbon[12] and, also, Gaertner and Kay[13] demonstrated the increased efficiency of screen surfaces over simple flat ones. The best explanation for this is that when a film

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From the Departments of Pediatrics, Surgery, and Medicine, Stanford University School of Medicine, San Francisco, Calif., and Cutter Laboratories, Fourth and Parker Streets, Berkeley, Calif.

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However, turbulence from a rough surface is not the only way to mix surface and deep blood in a filming system. There are probably many ways but one which we have found rather satisfactory in practice is to produce rapid changes in the thickness of the film and let the blood run down in rather thick waves one wave following the other. A smooth plastic surface on which a blood film is produced by a slowly moving oscillating jet allows blood oxygenation with approximately the same efficiency as a screen surface. We have, therefore, been able to produce a filming system in which blood is laid down on a disposable vinyl surface by a moving low pressure jet. This basic system appears to us to retain the desirable features of other filming systems and to have the great advantage that it can be essentially prefabricated and then disposed of after use.

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The Pumps and Catheters.—The pumps are the Gibbon type consisting of several parallel tubes pressed by a revolving pair of rollers. It is, therefore, several parallel pumps, depending on the number of tubes pressed by the same rollers. We use one tube or pump for each set of two or three lung-bags; all these pump-tubes being driven by the same roller, as shown in the diagram. A separate Gibbon roller-pump drives the arterialized blood back to the patient. The original Gibbon pumps were designed to press on rubber tubing, but we have modified ours to use disposable plastic tubing. Our basic flow pattern is essentially the Gibbon system. In use, the recirculating or oxygenating pump is set to run at a constant speed, while the arterial pump is either directly controlled by the operator or linked to the venous return by the automatic control system to be described below.

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*Manufactured by Cutter Laboratories, Fourth and Parker Streets, Berkeley, Calif.

Collection of blood from venae cavae has been through soft plastic catheters of appropriate size, introduced through purse-string sutures in the right atrium. These catheters come together to a Y-connector and drain by gravity to one end of the collecting manifold of the pump-oxygenator as shown in Fig. 2. A study of the flow diagram (Fig. 2) will show that venous blood cannot pass in any quantity from the venous end of the collecting manifold to the arterialized end without passing over the oxygenating film in the bags. Arterialized blood is collected from the other end of the manifold and passed through a combined filter and bubble trap. The return to the patient is through a stainless steel catheter in the femoral artery. All metal parts are treated with Monocote^{E}* prior to each use.

The Electronic Control System.—The lung-bags and their input and output tubes are held as described before in a Lucite-retaining frame. This frame is suspended from a pair of spring-steel arms with strain gauges placed at their bend-points. Essentially, these spring-steel arms form the bending beams of a delicate scale whose sensing element consists of the strain gauges. Weight of the entire system is indicated on a Brown indicator-controller which is electrically linked to a motorized variable transformer in such a way that if the weight on the entire lung unit with its blood reservoir drops below a preset value, the output rate of the arterial pump is proportionally reduced, until it is finally stopped. Therefore, the weight (hence the volume) of the blood in the lung and reservoir system controls the output of the arterial pump. If the amount of blood in the system decreases below the chosen setting, the output will be reduced and the level of blood in the lung will be maintained constant. This means that the arterial pump will not suck air if the input to the lung decreases so that the blood reservoir level falls, and it also allows the operator to maintain a very accurate balance between blood in the machine and blood in the patient.

Each pump is operated at a speed which can be manually varied by the operator. They are driven by direct current motors drawing power through appropriate rectifiers from an alternating current 110 volt source. Speed is controlled by variable transformers altering the voltage of the motor armatures. An alternate control-box, drawing from the hospital emergency direct current supply, has been provided in case of power failure.

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*Manufactured by Armour & Company, Division of Armour & Company, Kankakee, Ill.

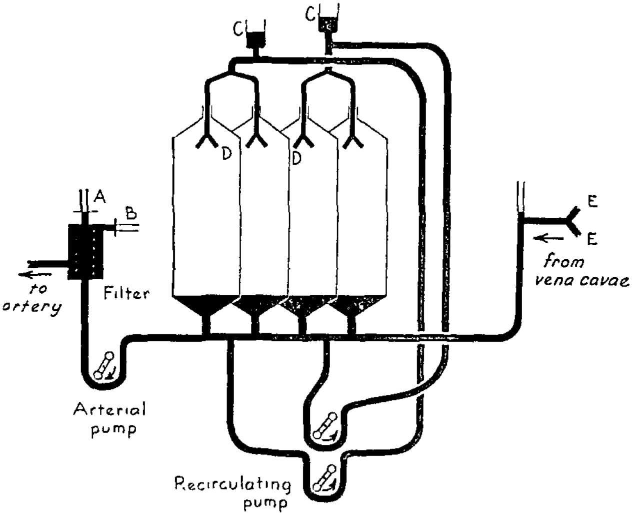

Fig. 1.—Diagram of flow.

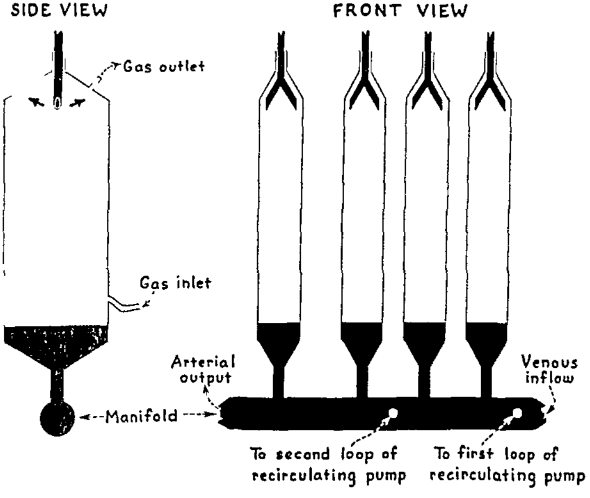

Fig. 2.—A single bag shown in detail and 4 bags shown in place, seen from the narrow edge.

TECHNICAL DETAILS OF APPARATUS AND PROCEDURE

The arterial pressure is monitored by polyethylene tubing inserted into the internal mammary artery. This avoids extra skin incisions and, once inserted, causes no further difficulties.

The venous pressure is monitored by a polyvinyl catheter inserted through the long saphenous vein in the groin. This vein is used for two reasons: because it is immediately adjacent to the femoral artery which is exposed for the arterial return from the pump and because it has been particularly valuable to leave this catheter in position for the first 24 hours. Concentrated solutions, such as 10 per cent calcium chloride, can then be given with no fear of thrombosis, as the tip of the catheter rests in the inferior vena cava. The conceivable hazard of emboli has not so far occurred in our experience. Removal of the catheter is performed with the patient in a slight Trendelenberg position, which is maintained for 10 minutes. Surprisingly, no troublesome hemorrhage has resulted from this maneuver.

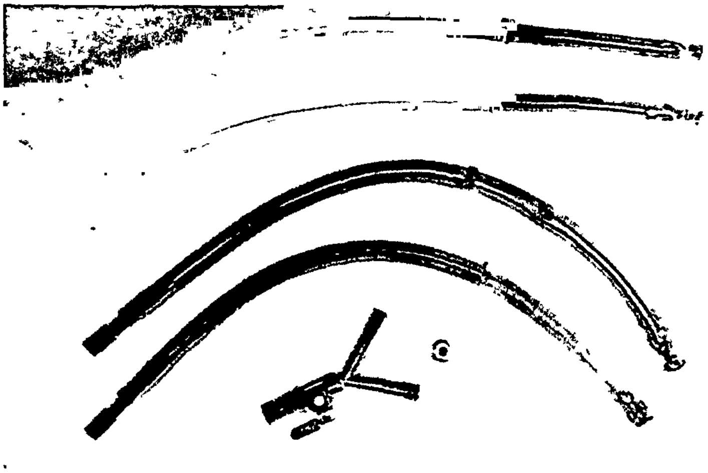

Fig. 3.—Two sizes of venous catheters with the Y-connectors. These have been autoclaved with small rubber band near tip. The fourth has been cut where the band was to form a whistle-tip ready for use.

For the withdrawal of blood from the venous side of the patient, polyvinyl catheters are chosen of a size as large as can be inserted into the vena cava via the right atrium. This is of considerable importance. Some difficulty was encountered in the earlier cases in this series, before the importance of a large venous return was realized. Any size tubing can be made to have a whistle-tip end if a constricting rubber band is placed around it before autoclaving. The end beyond the constriction is cut off right at the narrow point just before the catheter is used. Four large side holes are made near the tip of each tube. The catheters are joined to a length of 7/16 inch polyvinyl tubing by means of steel Y-tips with an air vent on the top. All air can be aspirated through this vent with a syringe. The air vent is equipped with a small occluding plug to prevent aspiration of air, if a tap is inadvertently opened (Fig. 3). The arterial side of the pump-oxygenator is connected to the patient by 5/16 inch polyvinyl tubing A steel catheter approximately 1½ inches long is inserted into the common femoral artery A set of various sizes of these catheters allows a suitable one to be chosen so that it is as large as can be easily inserted into the artery If too large a catheter is forced into the artery, it has been found that the stretching results in spasm proximal to the catheter and a lower flow is allowed than with a smaller catheter which slips in easily The insertion of a reasonably large catheter is assisted by careful dissection of the femoral artery and the use of papaverine, both of which prevent spasm of the vessel The catheter is tied in with heavy braided silk over a short piece of latex tubing to prevent damage to the vessel and it has been felt important that the similar tie which occludes the distal end of the artery should also be carried around the cannula to keep it aligned correctly in the wound We have not found it necessary to insert a long catheter into the femoral artery with its tip lying in the aorta, as a perfectly adequate flow can be maintained through a short catheter and this very shortness keeps the resistance as small as possible Steel catheters are connected by means of a short length of 5/16 inch polyvinyl tubing to a steel connector with an air vent on the top and then to the tubing from the machine Air is easily removed by means of a syringe from this point, small bubbles which adhere to the side of the tubing being dislodged by tapping the tubing with a clamp

Many of our fittings are adapted from those used at the Mayo Clinic All are the result of extensive trial and error Hard experience has taught us to give careful attention to small details of design and technique

CORONARY BLOOD RETURN

Most cardiotomies in this series were performed with induced cardiac arrest, using potassium citrate, so that the coronary venous return was reduced Yet, sometimes, even when the heart was stopped, there was a large intracardiac return from an aberrant vessel and, of course, when the heart was not stopped, coronary venous return was normal Rarely an intracardiac blood flow of up to 1 5 L per minute has to be sucked out of the open heart

When large flows have to be aspirated from the open heart, it is obviously necessary to return this blood to the general circuit In earlier work, we had difficulties following such large "coronary returns' which we felt might be attributed to air embolism from bubbles trapped in the sucked blood [15] We now believe that the return of aspirated blood must be treated as a major problem and must be carefully engineered

Two coronary suckers are available, one high pressure and one low pressure, either of which may be used depending upon the amount of coronary return One tip is specially adapted so that it can be left inside the heart near the largest source of blood such as inside the right atrium, the other is a slightly modified surgical suction tip for clearing the actual point on which the surgeon is working These two separate suction lines lead to separate pieces of tubing on a third Gibbon type pump, which discharge into a silicone coated glass reservoir Blood is allowed to stand in this reservoir as long as possible before being discharged back into the general circuit, to allow small bubbl [illegible] ways maintain several inches of blood in this reservoir, so as [illegible] be attributed to the method of bypass. In most experiments, there was no attempt to maintain sterility (because of personnel shortage). Several dogs died of infection several days after the operation. Using then the 2-day survival as the end-point, only one of the 13 animals died and this was an animal in which the tricuspid valve was removed surgically. He died rather rapidly in acute right ventricular failure. Each animal was subjected to ventriculotomy. The average duration of the ventriculotomy was 14 minutes. Seven out of the 13 animals went into ventricular fibrillation briefly when the blood was readmitted into the coronary arteries. This fibrillation either reverted spontaneously or was easily reverted to normal rhythm by electric shock. It was never a serious problem.

Results in Patients.—The apparatus has been used during intracardiac surgery on 70 patients. Details of these operations will be the basis of another communication. It is appropriate to say that this series of patients included both children and adults with diagnoses ranging from congenital heart disease to tumor of the heart. Some were in extremely poor condition when surgery was undertaken. Of these 70 patients, 18 died. The other 52 are living and improved or essentially cured. The great majority of deaths have been in patients with severe pulmonary hypertension, or in severe failure at the time of operation.

Severe bleeding has not occurred except in one case in which, on a second thoracotomy, a leak was found in the ventricular incision. The leak was repaired and the patient did well. Postoperative fever has rarely been a serious problem, although a temperature rise of 1° to 1.5° C. is rather common. The patients have usually been eating on the second or third postoperative day and have been ambulatory on the eighth or ninth day.

SUMMARY

A filming oxygenator which is almost totally disposable is described.

In basic plan, it resembles a Gibbon oxygenator, but the screen filming surfaces of the Gibbon lung have been replaced by disposable vinyl plastic bags.

In use in 70 patients, severe postoperative reaction or bleeding, traceable to the oxygenator, has not occurred.

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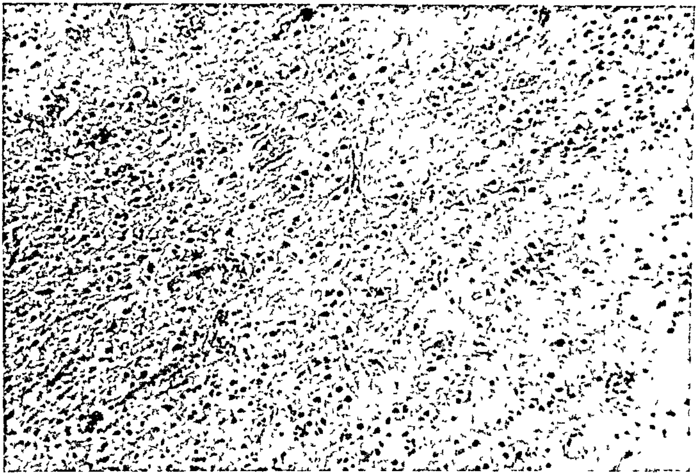

Fig. 2.—Recent necrosis of right parietal lobe of brain is shown along the left border.

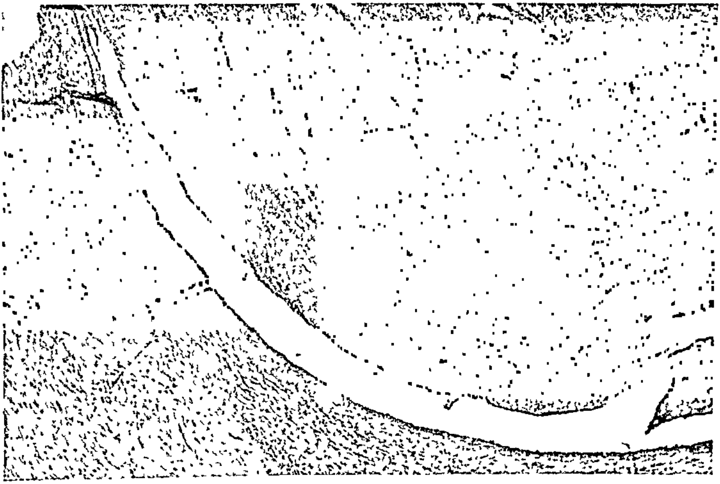

Fig. 3.—Recent unorganized mural thrombus of left atrial appendage.

peripheral infiltration of granulocytic leukocytes. Other pertinent findings were: subtotal hysterectomy, salpingectomy, ovariectomy, mild abdominal adhesions, pulmonary edema, congestion and atelectasis of the lungs, fatty metamorphosis of the liver, and atrophy of the islets of Langerhans.

DISCUSSION

After the advent of commissurotomy, attention was called to arterial embolism due to dislodgment of red thrombi from the left appendix. Later, it became evident that the same complication could be produced by freeing of bits of calcium following instrumental fracture of a calcified mitral valve. Technical devices have been adopted by Bailey and his associates[1] in order to reduce the frequency of this risk. In discussing his 20 cases of systemic embolization, occurring during or after operation, Ellis[1] described four factors accompanying arterial embolism in commissurotomy: (1) previous emboli, (2) auricular fibrillation, (3) thrombosis of appendage, and (4) calcific valve. He noticed also that the incidence of embolization increases when more than one factor is present. He stated that, in a total of 20 instances of embolization complicating valvotomy, 5 patients had calcific mitral stenosis as the only factor which could account for embolism. He gave no anatomic account of the type of embolism in such cases. In our case, there are two factors which can be considered as possible complicating phenomena: (1) the presence of red and gray left atrial thrombi, and (2) the calcification of the mitral valve. Histologically, the right cerebral artery, which had no arteriosclerosis at all, contained hyalinized, calcific material and a blood clot which was fresh and must be considered simply as a thrombus formed in situ once the embolic occlusion had occurred. The sections of the artery distal to this point contained a fresh clot, considered as the tail of the thrombus. In such an extensive infarction, we cannot exclude the possibility that the arterial occlusion was due to dislodgment of both atrial thrombi and calcific emboli. However, there is striking evidence that part of the embolus was formed by bits of calcium whose only source is to be considered the mitral commissure at the site where the fracture of the valve was performed. During the operation, before splitting the mitral commissures, the circulation through the carotid arteries was shut off. The patient was also considered to be in good condition postoperatively, even though it was difficult to make a definite statement because she was still under the effect of the anesthetic. It is possible that the embolism occurred within the first few hours following surgery. However, it might have occurred also during the operation and the embolus dislodged into the cerebral vessels through the incompletely closed carotid arteries. We do not know with certainty how great the threat of calcific emboli during or following commissurotomy might be. Probably such kind of emboli are much more frequent than is known, since serious effects occur only on lodgment in a few locations. Anyone who is familiar with fibrocalcific deformities of the mitral valve, in cases of chronic and healed rheumatic disease, knows how friable the calcific material is which is deposited in the mitral cusps and in the annulus fibrosus. We would like to call attention to the fact that such calcific deposits are dystrophic in nature and never become organized, probably because of the deficiency of blood supply to the valvular leaflets These deposits are easily sloughed off even with a minimal pressure by the examining finger, once the ring has been cut through or exposed by fracture

SUMMARY

A case of arterial embolism and ensuing cerebral infarction related to mitral valvotomy and proved to be the result of dislodgment of pieces of calcium from the calcific mitral ring, has been discussed A higher incidence of such a complication is probably to be expected considering the pathogenesis of such a type of embolism, in patients undergoing operative manipulation of a calcific valve of the heart

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TRAUMATIC VENTRICULAR SEPTAL DEFECT

Report of Two Cases

Gilbert S. Campbell, M.D., Robert Vernier, M.D., Richard L. Varco, M.D., and C. Walton Lillehei, M.D., Minneapolis, Minn.*

THE increased frequency of rapid deceleration accidents, the increased consciousness of possible cardiac trauma, and the successful surgical correction of congenital ventricular septal defects in numerous patients has resulted in a renewed as well as an increased interest in post-traumatic or acquired ventricular septal defects.

The first case in which the diagnosis was established by cardiac catheterization was reported by Guilfoil and Doyle in 1953[1] although, as early as 1847, Hewett reported 5 cases of rupture of the heart and large vessels as a result of injuries.[2] One patient in Hewett's report was a 5-year-old boy who was run over by a heavy cart which passed over his chest and the boy died 30 minutes later. Necropsy revealed a rupture of the ventricular septum at the union of the lower third to the upper two thirds of the septum through which the tip of the little finger could be passed. During the next 50 years other reports of a ruptured ventricular septum appeared and, in 1952, Pollock, Markelz, and Shuey[3] reviewed and reported 12 cases from the literature on this subject and added one case of their own. Other reviews or case reports have also been made.[4-10]

The purpose of this report is to present data on the first case of traumatic ventricular septal defects to be successfully closed surgically.[11] Also, we shall present follow-up information on another patient, the first case of diagnosis by cardiac catheterization,[1] who was subjected to a repeat cardiac catheterization recently at the University of Minnesota Hospitals.

CASE REPORTS

CASE 1.—A 13-year-old Negro boy was seen in the emergency room of the University of Arkansas Hospital on Sept. 11, 1954, with the following note from his referring physician in Pine Bluff, Arkansas: ''The above patient (C. R.) was admitted to Davis Hospital on August 16, 1954, following an accident in which he apparently was thrown from an ice truck, striking a bridge. On examination it was found that there was partial atelectasis of the left

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From the Departments of Surgery and Pediatrics, University of Minnesota Hospitals, Minneapolis, Minn.

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*Present address: University of Oklahoma Medical Center and Veterans Administration Hospital, Oklahoma City, Okla.

lung and the patient was spitting blood when he coughed. At this time a loud, harsh murmur could be heard all over the precordium and the second sound was faint but clear. His progress was slow but definite improvement was noted and he was discharged 8 25 54 to return to the office, which he did not do until today (9 11 54). At this time he appears to have congestion in both bases, an enlarged liver and an enlarged heart. The murmur has not changed. He is referred for diagnosis and treatment." On this visit to the emergency room he was thought to be in congestive heart failure, with marked cardiomegaly both clinically and radiographically. Unfortunately, he was not admitted to the hospital at this time. However, subsequently he was referred back again on Sept 14, 1954, at which time he was admitted to the Pediatric Service of University of Arkansas Hospital.

Admission History.—The boy (C. R.) was apparently in excellent health until the time of his accident on Aug. 16, 1954. He states that the rear wheel of the truck ran over his chest (although a witness denies this). He attempted to walk away from the scene of the accident but "blacked out" and was unaware of his surroundings until after he had been placed in Davis Hospital, where he remained 9 days. Following termination of hospitalization, he experienced mild orthopnea, mild exertional dyspnea, continued mild hemoptysis, questionable palpitation, and cough. All these symptoms were improving and he stated that he felt better at the time of his admission here than at any time since his accident.

Past History.—There was no history of previous symptoms or signs of rheumatic fever. The patient had had rare bouts of tonsillitis. He had had pneumonia at 2 years of age and he had had mumps and chickenpox. He was well developed, physically being larger than average in both height and muscular development.

Family History.—The patient is the youngest of twelve children. The rest of the history was not revealing.

Admission Physical Examination and Subsequent Course.—The patient was an extremely well developed and well nourished boy who was not in acute distress. There were moist râles at both lung bases. The point of maximal impulse was in the sixth left intercostal space at the anterior axillary line. A systolic thrill was palpable over the entire precordium. He had an extremely loud pulmonary second sound. The pulse rate was about 80 per minute, systemic blood pressure was 90/60 mm. Hg, and the respiratory rate 18 to 20 per minute. The liver could not be palpated but there was tenderness and muscle guarding over the liver area. There was a definite hepatojugular reflux. A slight amount of pretibial edema was present and there was distention of the neck veins. The patient could lie flat in bed fairly comfortably. A chest film taken on the day of admission revealed an enlarged cardiopericardial silhouette with evidence of congestive heart failure and minimal right pleural effusion. Hemogram was not remarkable; no anemia, leukocytosis, or elevated sedimentation rate was noted. The initial clinical impression was of rheumatic carditis with congestive heart failure, and the patient was digitalized and placed on a low salt diet. His response was very poor. Mercurial diuretics were relatively ineffective. Cortisone was given over a 2 week period, also, without visible response. In view of the continuing increase in the size of the heart, demonstrated on serial roentgenograms, the poor response to bed rest and digitalization, the persistent lack of anemia or leukocytosis, and an antistreptolysin O titer of 50 Todd units, it was thought that rheumatic carditis (which had never been an entirely satisfactory diagnosis) was unlikely and that perhaps traumatic heart disease was a possibility. Serial electrocardiograms had uniformly shown a first degree A-V block (Digitoxin had already been started when the first electrocardiogram was obtained) and persistent Q waves in Leads II, III, and AV_F, consistent with a posterior wall ventricular lesion.

On Nov. 19, 1954, 3 months after the accident, cardiac catheterization was performed and the results are shown in Table I.

The initial chest roentgenograms taken at Pine Bluff, Ark., at the time of the accident showed the cardiopericardial silhouette to be within normal limits as to size and contour.

On March 16, 1955, the patient, 13 years of age and weighing 55 Kg. was admitted to the University of Minnesota Hospitals for surgical correction of his traumatic ventricular septal defect. The findings described by the University of Arkansas were confirmed and on March 23, 1955, the patient was taken to the operating room. Upon opening the chest through a bilateral anterior thoracotomy (fourth interspace) with transverse sternotomy, numerous adhesions were encountered in the pleural spaces and between the parietal and visceral pericardium. An intense thrill was readily palpable low in the right ventricle. The patient was subjected to total cardiac bypass, utilizing a Sigmamotor pump and biologic membrane oxygenator.[11] Right ventricular cardiotomy revealed a *main defect low in the septum* near the apex of the heart which was the size of a quarter (measuring about 2.5 cm.). This defect had firm scarred margins unlike any congenital defects seen prior to that time or since. There were, in addition, two smaller satellite defects each 3 to 4 mm. in diameter in the immediate neighborhood. These defects were closed with multiple interrupted silk sutures (2-0). The duration of the total cardiopulmonary bypass was 20 minutes. The much enlarged heart immediately became visibly smaller and the thrill disappeared. Extracorporeal flow rates varied between 11 and 18 c.c. per kilogram in this 55 kilogram boy. Upon termination of the cardiopulmonary bypass, the arterial oxygen content was 22.7 volumes per cent, with an arterial blood pH of 7.1. Within an hour, the arterial pH had returned to a normal level as adequate correction of the septal defect with good postoperative circulatory state permitted a rapid and spontaneous correction of the metabolic acidosis by the patient. The patient awoke immediately from anesthesia and following an uncomplicated postoperative course was discharged from the University of Minnesota Hospitals on April 20, 1955.

TABLE I

SITE	PRESSURE, MM. Hg	OXYGEN CONTENT, VOL. %
Superior vena cava		9.2
Right auricle	+4/−4	8.9
Right ventricle	62/0	14.2
Pulmonary artery	70/24	14.1
Femoral artery		15.5
Systemic blood flow	2.40 L./min.	
Pulmonary blood flow	11.24 L./min.	
Shunt blood flow	8.76 L./min.	

The boy returned to Arkansas and on Aug. 17, 1955, had a cardiac catheterization performed at the University of Arkansas. The findings are shown in Table II.

TABLE II

SITE	PRESSURE, MM. Hg	OXYGEN CONTENT, VOL. %
Superior vena cava	6/3	15.6
Inferior vena cava	7/5	16.3-15.6
Right atrium	5/2	15.1
Right ventricle	28/0	17.7
Femoral artery		20.6
Systemic blood flow	2.90 L./min.	
Pulmonary blood flow	5.47 L./min.	
Shunt blood flow	2.57 L./min.	

It can be seen that the patient still has a small shunt postoperatively but his pulmonary pressures were now normal and his exercise tolerance has returned to normal. The transverse diameter of his heart was 19 cm. before operation and within 6 months postoperatively the transverse diameter of the heart had decreased to 16 cm. Postoperatively, he was not dyspneic after exercise and showed no signs of cardiac failure. However, there is some dyspnea with prolonged activity such as basketball playing.

CASE 2.—C. T., a 25-year-old ex-soldier was admitted to the University of Minnesota Hospitals on Jan. 9, 1957. He had been in an automobile accident on July 9, 1951, while on active duty in the armed forces and following this accident a ventricular septal defect was discovered. Catheterization findings of Aug. 29, 1951, have been previously reported[1] and are shown in Table III.

TABLE III

SITE	PRESSURE, MM. Hg		OXYGEN CONTENT, VOL. %
	INSTANTANEOUS	MEAN	
Superior vena cava	–	7	11.2
Right atrium	–	6.5	12.5
Right ventricle	27/6	15	
Right ventricle, mid			14.3
Right ventricle outflow tract			14.9
Pulmonary artery	27/15	21	
Pulmonary artery, main			14.3
Pulmonary artery, left			14.2
Systemic blood flow	6.0 L./min.		
Pulmonary blood flow	16.3 L./min.		
Shunt blood flow	10.3 L./min.		

Repeat cardiac catheterization was carried out at the University of Minnesota Hospitals on Jan. 10, 1957, and these findings are shown in Table IV.

TABLE IV

SITE	PRESSURE, MM. Hg	OXYGEN CONTENT, VOL. %
Superior vena cava		15.3
Right atrium, upper		15.8
Right atrium, mid		16.3
Right atrium, low	2	12.3
Right ventricle, mid	36/4	16.9
Pulmonary artery	14.4	17.8
Femoral artery		19.6
Systemic blood flow	5.9 L./min.	
Pulmonary blood flow	14.1 L./min.	
Shunt blood flow	8.2 L./min.	

It should be noted that the pulmonary artery pressure has not changed since the earlier catheterization 5½ years previously. Heart fluoroscopy revealed a normal transverse diameter, mildly accentuated pulmonary vascularity, and moderate right ventricular enlargement. He was diagnosed as having functional Class I to II heart disease.

DISCUSSION

Two cases of traumatic ventricular septal defect have been reviewed. In the first case the defect was such that the boy showed rather marked pulmonary hypertension with a large left to right shunt. This boy was in obvious cardiac failure and surgical closure of this defect was recommended and carried out. Postoperatively the boy has done very well although a small left to right shunt is still present. In retrospect, these multiple defects had very rigid and scarred margins (completely unlike the congenital lesions) and doubtless some space filling substance, such as compressed polyvinyl sponge, should have been placed (as would be done now) between the defect margins to stimulate deposition of connective tissue. However, the fact that the pulmonary pressures had returned to normal within 5 months after operation is ample indication that the residual leak was small and may close subsequently by deposition of fibrin. Since 3 years have now elapsed, a second postoperative catheterization is planned to test this thesis.

The second case is interesting in that the left-to-right shunt and the pulmonary artery pressure have remained at approximately the same levels as reflected by cardiac catheterization studies which were done 5½ years apart.

For the operated patient (C. R.), although the defects were located low in the muscular portion of the ventricular septum near the apex of the heart, pulmonary hypertension of a rather severe degree had developed rapidly (within 12 weeks), doubtless due to the large size of the shunt. This same situation has been seen a number of times in patients with congenital lesions during the past 4 years and we now know that a ventricular septal defect located low in the septum is not necessarily benign if large in size.

It is possible that most of these traumatic ventricular defects acquired by nonpenetrating trauma to the chest may be located low in the septum since the rupture probably occurs when the exit from the ventricles by way of the aorta or pulmonary artery is effectively occluded by the crushing force.

It is interesting to speculate whether the size and location of the defect in Case 2 may be of such a nature as to be hemodynamically different from congenital ventricular septal defects and from the acquired defects in Case 1. It is conceivable that pulmonary vascular changes may develop during the subsequent years in Case 2, although there is no indication thus far for any progression of the lesion as judged from his cardiac catheterization studies.

Surgical correction has been recommended to this patient as an elective procedure since the risk is now very low (1 to 2 per cent) and will restore the circulation to normal, obviating such potential complications as bacterial endocarditis or subsequent cardiac disability with the passage of time.

SUMMARY

The first patient in whom a traumatic ventricular septal defect has been successfully operated upon has been reported. An extracorporeal pump-oxygenator was utilized for the total cardiopulmonary bypass.

Additionally, a follow-up report, including a recent cardiac catheterization performed at this hospital, is made upon a second patient, of interest as it was the first case in which the diagnosis of a traumatic ventricular septal defect was made by cardiac catheterization.

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MANAGEMENT OF COARCTATION OF THE AORTA IN INFANCY

JD Mortensen, M.D., P. R. Cutler, M.D., W. R. Rumel, M.D., and
L. G. Veasy, M.D., Salt Lake City, Utah

THE GENERAL problem of coarctation of the aorta is rather well understood currently by most physicians and surgeons, thanks to the pioneer efforts of Gross,[15, 16, 17] Abbott, [1, 2] Edwards,[5, 12] and others. One phase of the coarctation problem, however, remaining poorly understood, hence controversial, concerns the infant in congestive heart failure associated with coarctation. The points of general agreement relative to such a patient are: first, coarctation of the aorta is a common cause of congestive heart failure occurring in the first year of life; second, when present, coarctation can usually be recognized clinically if considered and looked for in the infant who suffers from congestive failure; and third, congestive heart failure in infants who have coarctation of the aorta constitutes a serious situation with an extremely high mortality.

With this rather dismal note, general agreement and understanding of the problem deteriorates and we are left with considerable question as to the correct answer to such vital questions as: (1) what are the pathologic and physiologic explanations for the development of congestive failure in an infant with coarctation? (2) why is this lesion so difficult to manage successfully? and, (3) what are the best methods of management of a baby with coarctation and congestive heart failure? This communication summarizes our efforts to find answers to these three questions, utilizing two sources: a comprehensive review of medical literature comprising some 234 such case reports and a critical review of our own clinical experience with 20 such cases.

PATHOLOGIC AND PHYSIOLOGIC EXPLANATIONS

It appears evident that a completely satisfactory explanation for the development of congestive heart failure in infants with coarctation is not available in most cases. Obviously, most babies born with coarctation make satisfactory physiologic adjustments to the anomaly in utero or soon after birth, and symptoms only develop later as complications or sequelae from maintaining the abnormal physiologic state for a number of years. The oft-quoted suggestion[5] that postnatal closure of a patent ductus associated with coarctation creates an uncontrollable strain on the left ventricle, because the previously open ductus had prevented the development of sufficient collateral circulation, is effectively challenged by observation that in a considerable number of infants in severe

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From the Departments of Thoracic Surgery and Pediatrics, Latter-Day Saints Hospital, Salt Lake City, Utah, and the Rumel Chest Clinic.

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failure the ductus remains widely patent. Furthermore, a number of infants with congestive failure and coarctation have been demonstrated, either at operation or autopsy, to have well-developed collaterals. It seems doubtful, then, that a standard or predictable relationship exists between the degree of collateral circulation, patency of ductus arteriosus, and development of congestive failure in an infant with coarctation.

A factor of considerable significance, however, seems to be the coexistence of other serious cardiovascular anomalies in patients with coarctation. The incidence of associated serious defects in infants with coarctation, who develop congestive heart failure early, seems to be about 40 per cent,[10, 23, 26] while in patients whose coarctation remains asymptomatic until later life only about 15 per cent[2, 16] have serious associated cardiovascular anomalies. The compounding of two or more unphysiologic situations may precipitate congestive failure in early infancy, while a less abnormal physiologic state would permit the cardiovascular system to remain compensated for a longer time.

One would expect the degree of constriction present to play an important role in the ease with which congestive failure develops. However, there is no evidence at present available to indicate that either the narrowness of the constriction or the height of the systolic pressure can be correlated accurately with the time of development of congestive failure. Similarly, it would seem that existence of an anatomically high or long segment of constriction involving the arch of the aorta (the so-called infantile type of coarctation) should be a more serious disorder and cause earlier death. This is probably true. The fact remains, however, that most of the infants with coarctation and congestive heart failure have the short, ductal or postductal (so-called adult type) coarctation and the explanation for cardiac decompensation in such cases is not evident from anatomic observations alone.

A fourth factor that has received little attention in the literature, but in our experience may be important, is the basic biologic and environmental differences in patients. The frequency and severity of respiratory tract infections, the ability of the infant to resist infection, the home environment and hygienic care received, the inherent biologic vigor or toughness of the patient, and such related factors may play an important role in determining just which infant can make the necessary physiologic adjustments to avoid cardiac decompensation while another baby will succumb to heart failure, both having comparable anatomic defects.

REASONS FOR DIFFICULTY IN MANAGEMENT

Satisfactory explanations for the original development of congestive failure, as discussed above, would likewise go far to explain why management of these difficult problems is so often unsatisfactory. Until such understanding is achieved, we will probably be unable to explain fully the extreme difficulty with which these babies are carried through the first year or two of life. It appears evident, both from the literature and our own cases, that respiratory infections constitute particular problems in these babies. More often than not the onset of infection in the lungs or respiratory passages is accompanied by severe congestive failure. Surely, the respiratory infection makes recognition and management of cardiac decompensation more difficult. Similarly, with the common occurrence of feeding problems, the threat of aspiration, pneumonitis, malnutrition, and failure of proper growth and development the problem of management is further complicated.

An additional factor in this regard is the common failure of parents, as well as pediatric consultants, to maintain adequate digitalization. Once the baby seems to be doing well the tendency to omit the digitalis is ever present. With rapid growth of the child, the maintenance requirements of digitalis may vary considerably. It is well known that re-digitalization is commonly needed and that recurrent episodes of congestive failure will occur rapidly if extreme care and close observation are not carried out in each case.

Mention should be made of the difficulty in some instances in determining accurately the presence of cardiac decompensation in these infants. The clinical signs are not always detected with ease, and the differentiation of physiologic variations due to irritability, crying, or extraneous factors from pathologic signs of congestive failure or respiratory infection may pose real problems. If cardiac decompensation is not recognized and the patient is thought to be ill from pneumonia, digitalization and diuresis may be neglected or postponed. Similarly, if there is respiratory infection which is not recognized because of the preponderance of signs of congestive failure, adequate antibiotic therapy may not be instituted.

DEFINITIVE MANAGEMENT

All agree that the first consideration in an infant who is in congestive failure and has coarctation is the rapid and intensive administration of digitalis, oxygen, and diuretics. Similarly, all agree that ultimately the constricted segment of aorta should be corrected surgically, ideally at age 10 to 14 years. However, the pertinent question remains as to the best method of managing the infant once he has been digitalized, the infection controlled, and the diuresis accomplished. Should the baby be subjected to operation as a means of preventing further episodes of failure and decreasing the hypertension and cardiomegaly or should he be managed medically until 10 years of age before undergoing definitive surgery?

Until recent years, surgical repair of coarctation in infants under one year of age was considered technically impossible. In the last 5 years, however, sufficient experience has accumulated to demonstrate that the operation can be done, the risk is reasonable, and the results, although not perfect, are usually good. During this same period of time, the reports of results from medical management of such cases have changed from extremely pessimistic or hopeless[22, 23, 28] to generally fairly favorable[30] and an occasional optimistic attitude.[19]

Review of the literature up to December, 1957, reveals that 234 cases have been reported of coarctation and congestive heart failure in infants up to one year of age (Table I). In 35 cases, the diagnosis was not made before autopsy or for some other reason adequate treatment was not given and the patient died. In 134 cases, good medical management was given, including digitalis, antibiotics, and diuretics when indicated. Eighty-seven (64.9 per cent) of these patients died either in the initial or a subsequent episode of congestive failure. Sixty-five babies under one year of age have undergone surgical excision of the coarctation after digitalization had been carried out with 24 deaths (36.9 per cent mortality).

TABLE I. COLLECTED CASES OF COARCTATION OF AORTA WITH CONGESTIVE FAILURE DURING FIRST YEAR OF LIFE

MANAGEMENT (BIBLIOGRAPHICAL REFERENCES)	CASES REPORTED	DEATHS	MORTALITY (PER CENT)
Not recognized clinically, hence inadequately treated (Ref. 4, 5, 9, 10, 28, 32)	35	35	100
Medical treatment (Ref. 3, 8, 10, 14, 20, 23, 25, 26, 28, 30-32)	134	87	64.9
Surgical excision of coarctation (Ref. 3, 6, 7, 13, 14, 18, 20, 22, 23, 25, 27, 29, 31, 32)	65	24	36.9
Total Cases Reported	234	146	62.4

In our own experience (Table II) over the past 5 years, we have encountered 20 cases of coarctation in infants under one year of age. Four patients were asymptomatic and did not have congestive heart failure leaving 16 cases of coarctation and congestive failure in infants up to one year of age. Three were not recognized clinically and the patients died without adequate treatment. Five were treated medically, of which one (20 per cent) died. We have operated on 8 babies with coarctation and congestive failure under one year of age without a death.

TABLE II. TWENTY CASES OF COARCTATION OF AORTA IN INFANTS UNDER ONE YEAR OF AGE

MANAGEMENT	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
Not in failure, hence observation without treatment	4	0	0
Not recognized clinically, hence inadequately treated	3	3	100
Medical treatment	5	1	20
Surgical excision of coarctation	8	0	0
Total Cases	20	4	20

These figures, even though they must be viewed with some reservation because of the obvious failings of any such heterogeneous collective review, would seem to indicate that better results are obtained if infants with coarctation and congestive heart failure are treated surgically than by attempting to manage their cardiovascular problems medically for several years until a definitive operation can be done. This conclusion receives additional support by realization that even if the infant survives on medical management his heart rarely decreases significantly in size and the blood pressure in the arms and head remains elevated, often to a worrisome degree. On the other hand, most infants who have surgical correction experience normal or near normal blood pressure postoperatively and the heart size decreases, often dramatically (Figs. 1 and 2).

The possibility of stenosis at the anastomosis is real when excision is carried out in infants. This is known to have occurred in 7 of the 65 cases from the literature and is suspected in 2 of the 8 infants we have operated upon. It may be necessary in some of these cases for a second operation to be performed to achieve permanent relief of the aortic stricture, although we have not seen congestive failure redevelop following surgical correction of coarctation, even though a difference in blood pressure (signifying restenosis) between arms and legs may develop.

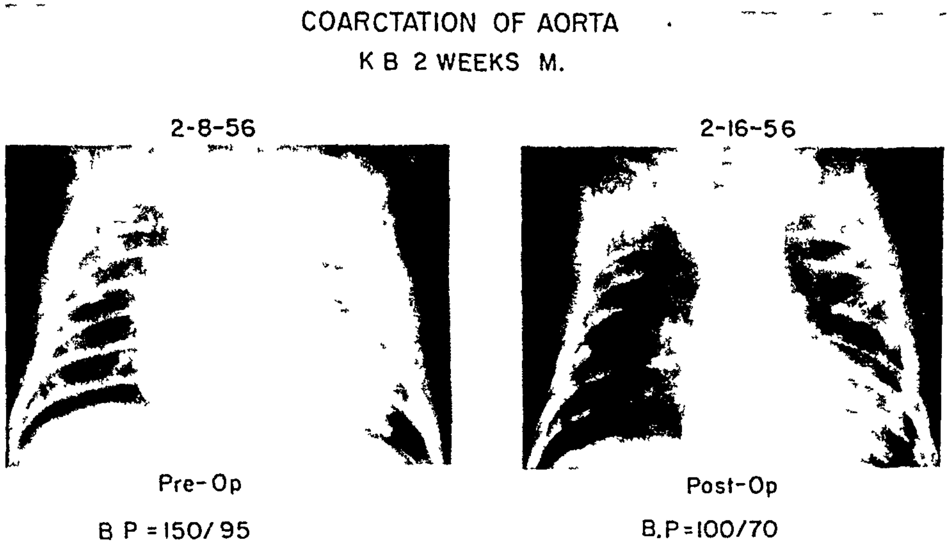

Fig 1.—Effect of surgical repair on heart size in an infant, 2 weeks of age, in congestive failure with coarctation of the aorta The preoperative film was taken after the patient had been digitalized Note the marked decrease in cardiac size one week later, after surgical repair.

In reporting 8 operations for coarctation in infants under one year of age without a death, we do not wish to minimize the magnitude and risk of the operation in these tiny infants. There are inherent dangers which must be recognized and dealt with properly or the operative mortality would become prohibitive. First, the operation must be done expeditiously, without tarrying. Infants do not tolerate long procedures well and we feel this procedure should not require more than 2 to 2½ hours if a satisfactory mortality rate is to be achieved. Fluid and electrolyte balance become matters of vital importance in these little patients and must be managed exactly. Respiratory difficulties, including atelectasis, pneumonitis, and laryngeal edema from the endotracheal tube must be prevented or treated vigorously. Technical details are important at the operating table, expert pediatric anesthesia is mandatory, and medical management by an alert pediatrician is essential if this type of surgery is to be accomplished successfully.

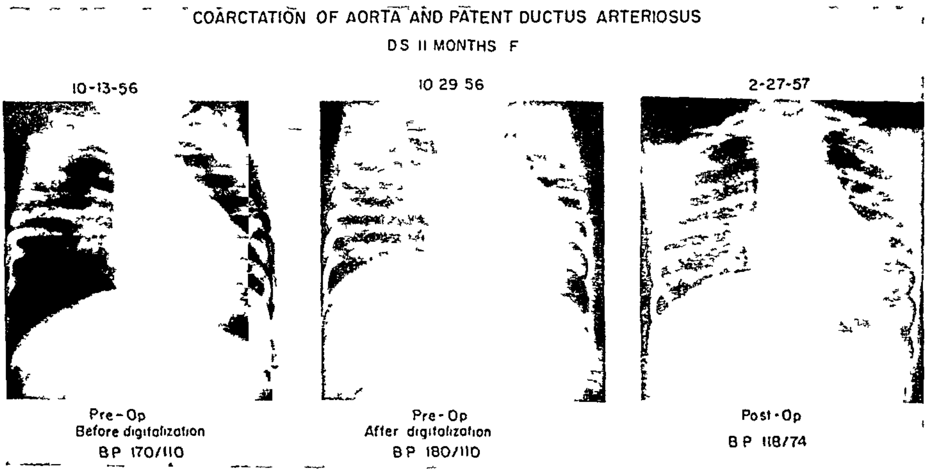

Fig 2.—Effect of surgical repair of coarctation and patent ductus arteriosus in an 11-month old patient in recurrent congestive failure. Note that heart size did not change significantly following digitalization but did decrease following surgical correction. Note also the decrease in pulmonary vascular engorgement following closure of the patent ductus arteriosus.

SUMMARY

Although we frankly admit our conclusions are tentative and may be modified with added experience, our current practice, based on the considerations mentioned above, is as follows: If coarctation of the aorta is discovered in infants who are doing well generally and have no evidence of congestive heart failure, the patient is followed carefully without medication but with close supervision until approximately 8 years of age when surgical excision of the coarctation is carried out. Every infant with evidence of congestive heart failure is examined carefully for signs of coarctation of the aorta. When coarctation is recognized in such an infant in congestive failure, intensive medical management with digitalis, diuretics, and antibiotics, when indicated, is carried out. If clinical response to medical management is excellent, if blood pressure in the arms is under 150 systolic, if the heart is not grossly enlarged after complete digitalization, and if circumstances permit a good long-term medical program with frequent recheck examinations, we will consider deferring definitive surgical treatment until later childhood, the patient being carefully followed on a strict medical regimen. All other infants with coarctation of the aorta who have been in congestive heart failure are considered best treated by surgical excision of the coarctation. Furthermore, if congestive failure recurs in a patient being managed medically, surgical treatment is then recommended. Our present indications for recommending surgical intervention in an infant with coarctation who has been in congestive heart failure are thus summarized as follows (Table III): first, when medical control of decompensation is unsatisfactory; second, when decompensation recurs on a satisfactory medical program; and third, in an occasional patient as an elective measure when poor medical control is anticipated.

TABLE III. INDICATIONS FOR SURGERY IN INFANTS WITH COARCTATION OF AORTA AND CONGESTIVE FAILURE

INDICATION	NUMBER OF CASES
Congestive failure in first month of life, *unsatisfactory medical control* (Operated early, more or less of necessity)	4
Repeated episodes of congestive failure in first year of life; each episode responded to intensive medical regimen *but poor maintenance control* (Operated late, as elective means of maintenance management)	3
Single episode of failure at one month of age, responded well to medical treatment (Operated electively *to prevent further symptoms*)	1
Total Operated Cases	8

CONCLUSIONS

1. Coarctation of the aorta is a common recognizable cause of congestive heart failure during the first year of life.

2. Prognosis of an infant with coarctation who develops congestive failure during the first year of life is rather grave.

3. Under ideal circumstances, certain infants with coarctation of the aorta and congestive failure can be managed by a carefully controlled medical regimen until later childhood when definitive surgical treatment should be carried out.

4 Nevertheless, most infants with coarctation who develop congestive failure during the first year of life will be better managed by surgical repair of the coarctation after adequate medical preparation

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REPLACEMENT OF THORACIC AORTA WITH ALCOHOL-PRESERVED HOMOGRAFTS

Thomas C. Moore, M.D., and Angelo Riberi, M.D., Indianapolis, Ind.

THE PRESERVED arterial homograft has played an important role in the development of currently employed techniques for arterial replacement and bypass. Although the synthetic arterial prostheses have largely supplanted the use of preserved homografts, considerable clinical interest still exists in the ultimate fate of arterial homografts and in any possible relationship between the method of preservation and this fate.

The suitability of 70 per cent ethyl alcohol for the sterilization and preservation of homografts in experimental small artery replacement was reported by the authors in 1956.[2] The results with alcohol preservation were comparable with those encountered when freeze-drying techniques were employed. Except for the study of Kimoto and his associates[1] in 1954, relatively little has been published in recent years relative to the use of alcohol for homograft preservation and sterilization.

The purpose of this report is to record the results of the experimental use of alcohol-preserved homografts of aorta for replacement of proximal descending thoracic aorta. The gross and microscopic appearance of the homografts was studied at varying intervals, from one day to one year, after placement. The replaced segment of thoracic aorta was utilized to replace a section of the animal's superior vena cava. The suitability of the fresh autogenous aorta, thus obtained, for superior vena caval replacement has been reported in greater detail elsewhere.[3]

MATERIAL AND METHODS

Healthy mongrel dogs were used. The weight of the dogs ranged from 12 to 23 Kg. A mixture of oxygen and ether, delivered through an endotracheal tube by means of a mechanical respirator, was employed for anesthesia following induction with intravenous Pentothal. Hypothermia was achieved by immersion of the anesthetized and intubated dog in an ice water bath. The body temperature generally was lowered to approximately 31° C.

From the Department of Surgery, Indiana University Medical Center, Indianapolis, Ind.

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A left thoracotomy was carried out through the fourth or fifth intercostal space. The more cephalad portion of the descending thoracic aorta was dissected free from surrounding structures. The intercostal arteries in this area were divided between ligatures. The aorta was occluded with Potts coarctation clamps above and below the sites of proposed transection. The isolated segment of aorta was resected. The resected section of aorta generally measured between 6 and 8 cm. in length. The resected aorta was replaced with an alcohol preserved aortic homograft of approximately the same length. The duration of homograft storage and preservation in 70 per cent ethyl alcohol ranged from 6 to 21 days. The alcohol preserved homografts were reconstituted for one hour prior to use in a normal salt solution containing streptomycin and penicillin. The anastomoses were carried out with a continuous over and over 5-0 arterial silk suture. In all of the animals the homograft appeared to function satisfactorily on completion of the anastomoses and removal of the occluding Potts clamps. The homograft was covered with adjacent pleura and the left chest was closed in layers. A catheter was left in the left chest for subsequent aspiration.

The resected segment of aorta was used to replace a segment of superior vena cava through a right thoracotomy. Following this procedure, the dog's temperature was returned to normal by immersion in a warm water bath. Upon completion of the rewarming, both chest catheters were aspirated and withdrawn. Penicillin was given for 4 days following operation.

RESULTS

The proximal descending thoracic aorta was resected and replaced with an alcohol preserved aortic homograft as described in 31 dogs. The patency and the gross and microscopic appearance of the homograft were investigated in all animals on postmortem examination from one day to one year following operation.

The homograft had remained patent in all of the animals (Table I). In only one animal was there a significant reduction in the size of the lumen. In this animal (Dog 821), a large thrombus on the wall of the graft had produced a 30 per cent reduction in the lumen of the graft 3 months following operation. Although the periods of alcohol storage were relatively short, there was no apparent affect of the period of preservation on the ultimate fate of the homograft. There was no evidence of homograft induced infection.

The duration of homograft placement seemed to be the most important factor in the fate of the grafts. Little significant change was encountered in the gross appearance of the homograft during the first month after operation. However, in the interval from 1 to 4 months, gross alterations in the graft were found to occur in a high per cent of the animals. The principal changes were those of intimal roughening and erosion and thrombus formation. A different type of gross change was found in animals sacrificed between 11

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TABLE I. SUMMARY OF RESULTS OF EXPERIMENTAL USE OF ALCOHOL-PRESERVED HOMOGRAFTS OF AORTA FOR REPLACEMENT OF THORACIC AORTA

DOG NO.	INTERVAL OPERATION TO AUTOPSY	PERIOD OF HOMOGRAFT STORAGE IN ALCOHOL (DAYS)	GRAFT PATENCY	REMARKS
806	1 day	9	Patent	
836	1 day	21	Patent	
838	1 day	9	Patent	
845	1 day	9	Patent	
855	1 day	9	Patent	
824	2 days	10	Patent	
822	3 days	9	Patent	
876	5 days	6	Patent	
895	5 days	6	Patent	
808	7 days	9	Patent	
843	7 days	13	Patent	
888	8 days	14	Patent	
839	12 days	9	Patent	
825	14 days	21	Patent	
812	30 days	15	Patent	
817	33 days	11	Patent	Intimal roughening
853	34 days	16	Patent	Intimal roughening with areas of thrombosis
887	34 days	14	Patent	Thrombus on graft wall
855	37 days	16	Patent	
831	2 mo.	16	Patent	Intimal roughening with areas of thrombus formation
842	2 mo.	9	Patent	Thrombus on graft wall
871	3 mo.	12	Patent	Intimal roughening with areas of thrombus formation
787	3 mo.	11	Patent	
821	3 mo.	6	Patent	Large thrombus on wall with reduction in size of lumen
813	4 mo.	15	Patent	Intimal roughening with areas of thrombus formation
828	7 mo.	15	Patent	
851	11 mo.	6	Patent	
862	11 mo.	16	Patent	Extensive calcification of graft with early aneurysm formation
872	11 mo.	12	Patent	Areas of graft calcification
826	12 mo.	15	Patent	Extensive atheromatous degeneration with dilatation of graft
827	12 mo.	15	Patent	Areas of graft calcification

and 12 months following operation. Atheromatous degeneration, calcification, and graft dilatation were the gross alterations discovered in 4 of the 5 animals in this group (Fig. 1).

It is of interest that the resected segment of fresh autogenous aorta which was used for superior vena caval replacement had not only remained patent in all of the animals but also had remained free of degenerative changes, calcification, fibrotic narrowing, dilatation, and thrombus formation in all. To illustrate this observation, it may be noted that the gross appearance of the fresh autograft of aorta in the critical area of superior vena caval grafting contrasts sharply with the appearance of the alcohol-preserved homograft of aorta utilized in the less critical area of aortic replacement in the same animal (Dog 862) one year after operation (Fig. 2).

Microscopic study of the homografts revealed rather constant findings. The grafts remained acellular and relatively amorphous. The amorphous appearance increased with the passage of time and was associated with a significant decrease in the thickness of the graft wall (Fig 3) There was no evidence, in any of the sections studied, of significant vascular or cellular ingrowth into the homograft, either from the host artery at the site of anastomosis or from the living host tissues adjacent to the outer wall of the graft (Fig 4)

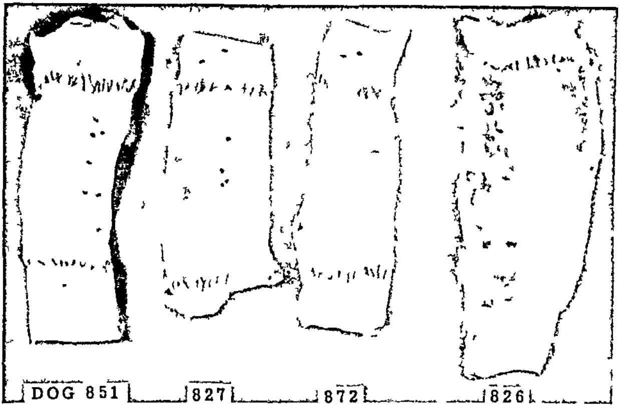

Fig 1—Photograph showing the appearance of four alcohol preserved aortic homografts used to replace resected segments of thoracic aorta at autopsy, 11 and 12 months after operation

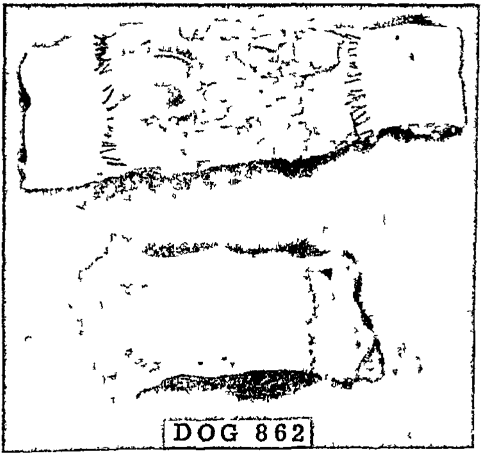

Fig 2—Photograph of aortic homograft used for aortic replacement (*above*) and aortic autograft used for superior vena caval replacement (*below*) in same animal 11 months following operation The extensive calcification and aneurysmal dilatation of the homograft are in marked contrast to the normal appearance of the autograft.

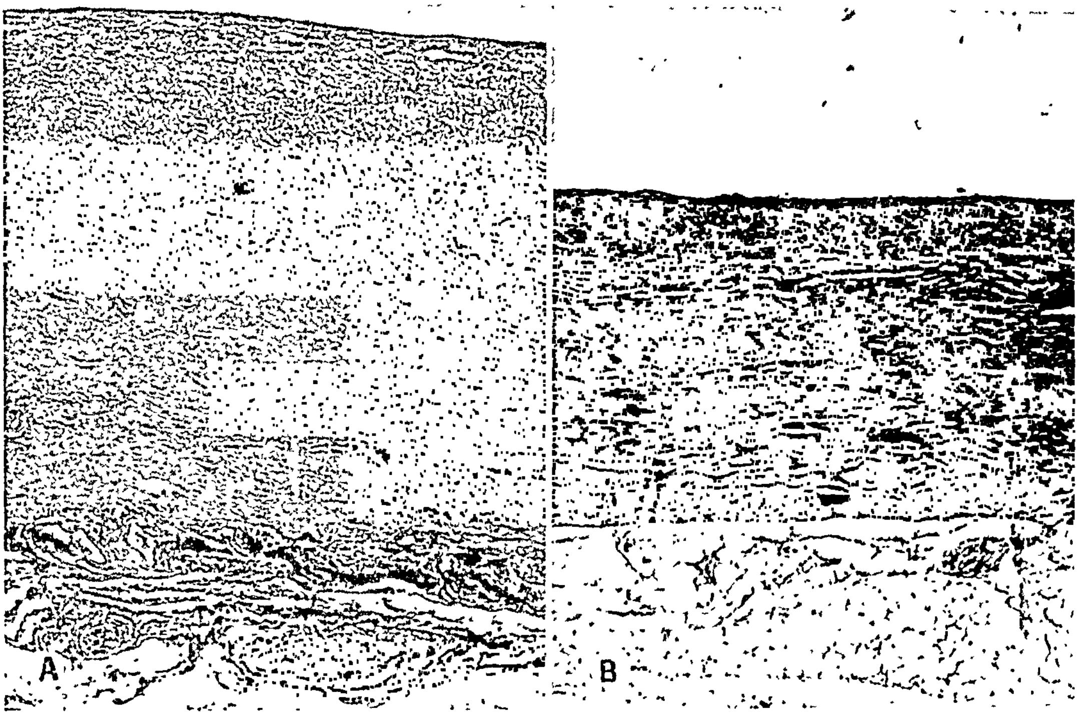

Fig. 3.—Photomicrographs, at the same magnification, illustrating the degree of homograft thinning (*B*) in comparison with adjacent normal host aorta (*A*), 12 months after graft placement.

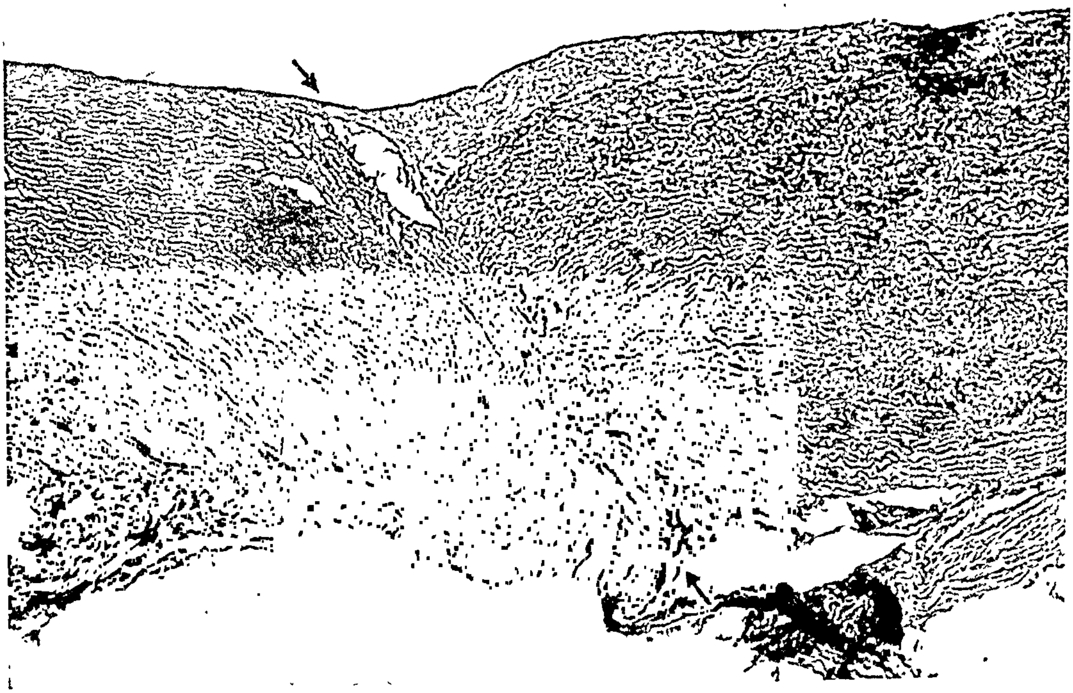

Fig. 4.—Photomicrograph showing junction line (*arrows*) between homograft (*left*) and host aorta (*right*), 12 months after operation. There is no vascular or cellular ingrowth into the homograft from either the host aorta or adjacent host connective tissue.

DISCUSSION

The observation in this study that all 31 alcohol preserved aortic homografts remained patent in the thoracic aorta from one day to one year after placement suggests that the alcohol method of preserving aortic homografts may be, at least, as suitable as the freeze drying method The period of time the grafts were stored in alcohol, within the limits of this study, did not appear to affect the fate of the grafts Similar findings were recorded by Kimoto and his associates[1] in 1954 They employed both 70 per cent ethyl alcohol and pure ethyl alcohol for aortic homograft preservation and utilized periods of graft storage in these concentrations of alcohol ranging from 9 to 269 days An analysis of their reported results reveals the two concentrations of alcohol to be equally effective The period of storage in their study did not appear to be a factor in the success or failure of the graft with respect to the retention of patency Twenty of the 22 alcohol preserved aortic homografts used by them for aortic replacement remained patent Only 6 of their animals were followed in excess of 100 days

While retention of graft patency does not seem to be a problem in the replacement of segments of thoracic aorta with homografts, the occurrence of degenerative changes with the passage of time does pose some real problems These degenerative changes include calcification thinning and dilatation of the graft The relatively amorphous, acellular character of the graft and its apparent "sequestration" from surrounding host tissues, with the absence of host vascular and cellular ingrowth, were regarded as significant factors in the development of these changes Szilagyi and his associates[4] have recently reported similar disturbing changes in human arterial homografts

The degenerative homograft changes encountered in this study fell into three rather distinct periods Little alteration in the gross appearance of the graft was found in the first month after operation, whereas grafts examined between 1 and 4 months after placement showed a high incidence of intimal erosion and ulceration and thrombus formation These changes were not encountered in grafts examined 11 and 12 months following operation In these grafts, the significant degenerative changes were those of graft thinning with localized or general dilatation, atheromatous plaque formation, and calcification

An unusual opportunity was offered in this study to compare the fate of free grafts of fresh autogenous aorta and that of preserved homografts of aorta when both types of graft were used for vascular replacement in the same animal The fresh autografts were employed with success in the superior vena cava, a critical area for vascular replacement where homografts of aorta have been shown to be unsuitable The fresh autograft, with its structure and cells intact, remained a part of the living organism and its superiority was indicated by its freedom from the progressive degenerative changes which afflicted the great majority of the alcohol preserved homografts

SUMMARY

The use of alcohol-preserved homografts of aorta for the replacement of 6 to 8 cm. resected segments of proximal descending thoracic aorta in 31 dogs is reported. In all animals, the homograft was patent at the time of postmortem examination, from one day to one year after operation. Despite this satisfactory retention of graft patency, a number of disturbing degenerative changes were discovered in a large per cent of grafts examined over one month after placement. Intimal erosion and ulceration with thrombus formation were encountered in the early months after operation, while graft thinning and dilatation with calcification and atheromatous plaque formation occurred later. There was no microscopic evidence of vascular or cellular ingrowth in any of the grafts studied and the homografts appeared to be, in effect, "sequestered" from the host organism. The fate of the alcohol-preserved aortic homograft in the thoracic aorta is compared with that of the free graft of fresh autogenous aorta used for superior vena caval replacement in the same animal.

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STUDIES OF THE CORONARY CIRCULATION

I. The Surgical Anatomy of the Right Coronary Artery of the Dog and the Effects of Acute Ligation

Knut Haeger, M.D., Malmö, Sweden*

THE ANATOMY of the coronary arteries in the dog has been studied by several authors[2, 6, 7, 10]. These authors generally agree that the right coronary artery arises from the aorta near the right anterior cusp, and runs in the atrioventricular groove where it bifurcates into two main branches. One branch runs along the anterior portion of the right ventricle and the margo acutus. The other runs to the posterior part of the right side of the heart. Pianetto states the external diameter of the main stem of the artery is between 1.0 and 1.5 mm.

Acute ligation of the right coronary artery generally causes severe trouble. Porter[11] ligated the right coronary artery in 11 dogs and observed cardiac standstill. In 2 animals, cardiac standstill was followed by ventricular fibrillation. The ultimate fate of the dogs surviving the acute insult was not reported by the author. Cohnheim and von Schultess Reichberg[1] regularly observed ventricular fibrillation after the ligation of either of the two major coronary arteries. Smith[11] ligated the right coronary artery of 8 dogs. He noted four immediate and three late deaths, one animal survived in excellent condition. Paradé[8] ligated the artery of 5 dogs, one died of ventricular fibrillation, and the other 4 died within 48 hours. Donald and Essex[2] ligated the right artery in 21 dogs, 5 of these died within 48 hours after the operation. However, 16 of their dogs survived in good condition. The wide variation in the incidence of ventricular fibrillation and early death found in the above papers is probably explained by a recent report by Milch and associates. These authors reported that, following ligation of a major coronary artery, any slight somatic stimulation readily induced ventricular fibrillation. Also Gianelli and co-workers[3] stress the many variables of acute ligation of a coronary artery and the different results that may be obtained by different operators.

The purpose of the present report is twofold. We wish to describe is apparently a common variant of the classical description of the extr

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*Halsted Fellow at the University of Colorado School of Medicine, Denver, the Department of Experimental Surgery, Allmänna Sjukhuset, Malmö, Sweden.

distribution of the right coronary artery. In addition, we wish to demonstrate the consequence of this anatomic variation on the effect of acute ligation of the right coronary artery and some of its branches.

METHOD

This report includes observations on 90 dogs; 83 were mongrels and 7 were trained greyhounds. All animals were anesthesized with intravenous Nembutal in a dosage of approximately 30 mg. per kilogram and were artificially respired with oxygen by means of an automatic, intermittent positive pressure respirator. All operations were performed under completely aseptic conditions. The chest was entered by way of right thoracotomy at the level of the fourth or fifth interspace. After slitting the pericardial sac, the extramural anatomy of the right coronary artery was noted. Any variant from the classical description of this vessel was sketched immediately following surgery.

After tracing the course of the right coronary artery, either the main stem itself or one or more of its branches was ligated. Since these experiments were undertaken as a control to other experiments involving the insertion of a plastic tube into the right coronary artery, those animals subjected to ligation of the main branch of the right coronary artery were also subjected to manipulations simulating the insertion of a plastic tube into the artery. We have called this a sham operation.

Following this procedure the animal was watched for a short period of time to see whether early ventricular fibrillation developed. The thoracotomy was closed, and the animal was given supportive postoperative care. Only those animals surviving in good health for periods of longer than 7 days were included as survivors. Those animals succumbing to late death were autopsied to determine presence or absence of myocardial infarction.

RESULTS AND DISCUSSION

The Anatomy of the Right Coronary Artery.—As a rule, the distribution of the right coronary artery was found to be in complete agreement with the observations of the authors just quoted. In most of the animals, the branches were distributed as shown in Fig. 1 and diagrammatically in Fig. 2, *A*. The two dominant branches of the artery are the ramus marginalis acuti (No. 5 in Fig. 2) and the ramus circumflexus dexter (No. 7 in Fig. 2). In some dogs, however, the ramus ventriculi dexter anterior (No. 4 in Fig. 2) was very well developed, whereas the ramus marginalis acuti was less pronounced. This distribution is depicted in Fig. 2, *B*. Table I shows that, of the 83 mongrel dogs observed, the ramus ventriculi dexter anterior was the dominant anterior branch of the right ventricle in only three instances. However, this was the dominant anterior branch in all 7 of the greyhounds observed. This difference in right coronary distribution, greyhound versus classical, has certain surgical implications which shall be discussed later.

TABLE I DOMINANT ANTERIOR BRANCH OF THE RIGHT CORONARY ARTERY OF THE DOG

"SPECIES"	NUMBER	DOMINANT ANTERIOR BRANCH	
		RAMUS MARGINALIS ACUTI	RAMUS VENTRICULI DEXTER ANTERIOR
Mongrels	83	80	3
Greyhounds	7	0	7
Totals	90	80	10

In most of the dogs observed, the diameter of the main stem of the right coronary artery was within the limits stated by Pianetto[9] In some dogs, however, the external diameter of the artery was found to exceed 2 mm and, in a few cases, a plastic tube with an outside diameter of 2 43 mm could be easily threaded into the lumen

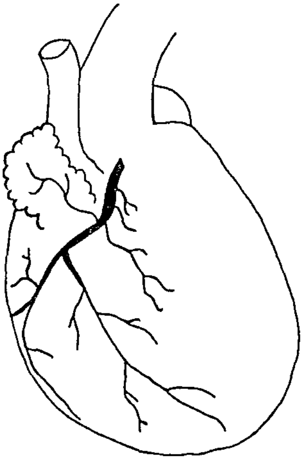

Fig 1—The normal anatomy of the right coronary artery in the dog The right auricular appendage is turned upward to expose the proximal part of the artery

The Effects of Acute Ligation of the Right Coronary Artery—The results of 16 sham operations, including complete acute ligation of the right coronary artery, are shown in Table II Thus, in this series, 15 out of 16 dogs died within the first 24 hours after ligation, and in 4 of the 5 animals surviving the operation, right myocardial infarction was present at autopsy

TABLE II RESULTS OF SHAM OPERATION INCLUDING TOTAL ACUTE LIGATION OF THE RIGHT CORONARY ARTERY

FATE OF THE DOG	NUMBER OF DOGS
Ventricular fibrillation	11
Died within 24 hours	4
Survival	1

During the course of our experiments, it was observed that no harm followed ligation of the smaller branches originating from the proximal e the artery (Nos. 2, 3, and 10 in Fig. 2). Branch No. 2 was ligated five times, No. 3 was ligated in 60 dogs, and No. 10 in 40 dogs. In no instance did these ligations result in alteration of cardiac rhythm or in the development of myocardial infarction.

The procedure for placing a tube in the right coronary artery, to be described in a subsequent paper,[1] requires ligation of the ramus ventriculi dexter anterior (No. 4 in Fig. 2). This vessel was ligated in 80 animals in which the dominant anterior branch was the ramus marginalis acuti. In none of these animals was there either a disturbance of heart rhythm or gross signs of myocardial infarction noted. In the greyhounds, however, where this branch was extremely well developed and probably supplied a comparatively large part of the wall of the right ventricle, ligation of this branch caused either immediate ventricular fibrillation or subsequent myocardial infarction in the area supplied by this vessel. Thus, in all dogs with the typical "greyhound anatomy," ligation of the ramus ventriculi dexter anterior resulted in ventricular fibrillation or early postoperative death from myocardial infarction; whereas ligation of the same branch in dogs with the classical described anatomy of the right coronary artery caused no harm.

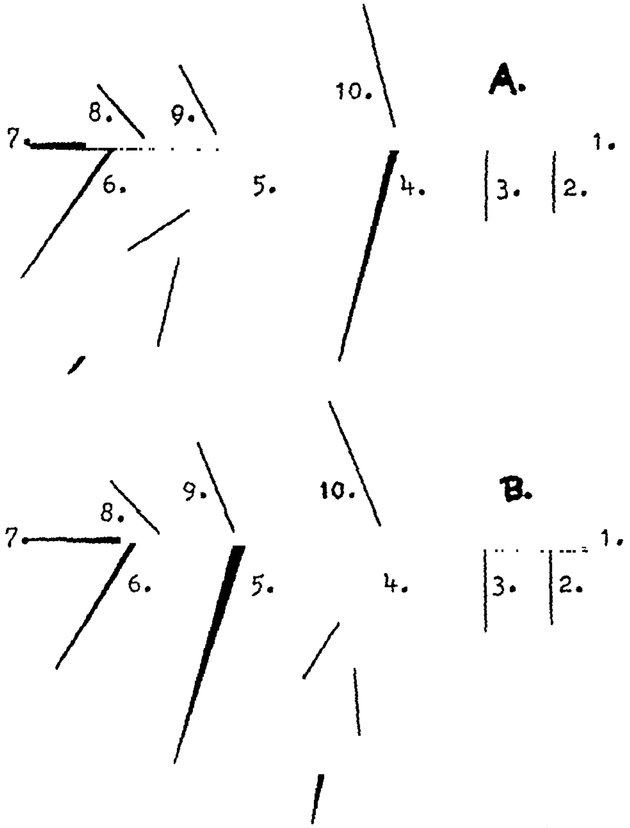

Fig. 2.—Diagrammatic representation of the right coronary artery.
A, Normal dog.
B, Dogs with "greyhound" anatomy.
1—Art. coronaria cordis dexter; *2* and *3*—Small branches; *4*—R. ventriculi dexter anterior; *5*—R. marginalis acuti; *6*—R. ventriculi dexter posterior; *7*—R. circumflexus dexter; *8* and *9*—Small branches; *10*—R. atrialis dexter anterior.

CONCLUSION

Observations on the anatomy of the right coronary artery of 90 dogs confirmed the findings of earlier authors. In some dogs, however, notably the trained greyhound, the ramus ventriculi dexter anterior is the dominant anterior branch of the right coronary artery rather than the ramus marginalis acuti. In those dogs with "greyhound" anatomy, ligation of the ramus ventriculi dexter anterior uniformly resulted in death.

Under the conditions of these experiments acute ligation of the main stem of the right coronary artery resulted in ventricular fibrillation or death by myocardial infarction in 15 of 16 dogs. No detrimental effect was noted following ligation of the three branches of the right coronary artery that arise proximal to the ramus ventriculi dexter anterior.

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STUDIES OF THE CORONARY CIRCULATION

II. Nylon and Polyethylene Tubes as Coronary Artery Prostheses

Knut Haeger, M.D., Malmö, Sweden, Georg R. Wallgren, M.D.,** Helsingfors, Finland, and Peter Dundas, M.D.,*** Denver, Colo.*

During the past few years many nonbiologic materials have been used as replacements in peripheral artery disease. As a rule, the initial results of the operations have been fair; however, all types of grafts have shown a high incidence of late thrombosis or, in some cases, rupture of the graft. Recent results with the Edwards-Tapp chemically-treated nylon prosthesis seem to be better than with other materials.[3, 5] On the other hand, it was recently stated that plastic materials nearly always fail in small arteries.[12]

In attempts to revascularize the ischemic myocardium, several surgical procedures have been tried. As yet, however, none of these have been generally accepted. Recently, some work was published on the utilization of plastic material tubes for the revascularization of the heart. Smith and coworkers[20] connected the aorta with the myocardium by means of a 4.5 mm. diameter nylon tube and reported good anatomic and functional results with roentgenologic evidence that the tube remained open. Massimo and Boffi[11] created an anastomosis between the cavity of the left ventricle and the myocardium in dogs by means of a polyethylene T-tube with successful results in 32 experiments. In a preliminary report of this study,[6] it was stated that a polyethylene tube inserted as a bridge in the resected right coronary artery stayed open at least 9 months after the operation, and contrast medium injected in the root of the aorta in the living dog could be demonstrated distal to the graft.

Attempts have been made to direct the blood flow from systemic arteries to the distal parts of the occluded coronary arteries. Thus, as early as in 1940, Murray[13] reported on successful coronary artery anastomoses from the internal mammary artery in dogs. Thal and associates,[23] using a temporary

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*Halsted Fellow, University of Colorado School of Medicine, Denver, Colo., from the Dept. of *Experimental Surgery*, Allmänna Sjukhuset, Malmö, Sweden.

**Foreign Exchange Student of the Institute of International Education from Helsingfors, Finland.

***Halsted Fellow, University of Colorado School of Medicine, Denver, Colo., from Oslo, Norway.

coronary perfusion via a plastic cannula made an end-to-end internal mammary to coronary artery anastomosis in dogs. With coronary arteriography, they were able to demonstrate the anastomosis to be patent in 7 dogs out of 17 after an observation time of 2 to 6½ months.

In the present study an attempt has been made to evaluate experimentally the fate of polyethylene and nylon tubing replacements of the right coronary artery of the dog.

OPERATIVE TECHNIQUE

Mongrel dogs, varying in weight from 14 to 40 Kg., were used. The dogs were anesthetized with intravenous pentobarbital sodium (30-40 mg. per kilogram of body weight) and, after tracheal intubation, artificially controlled respiration using 100 per cent oxygen was maintained. The right side of the heart was exposed by right-sided thoracotomy with the subject in the left lateral position. To some of the dogs procaine amide (Pronestyl*) was given in intravenous dextran infusion; in other experiments the dogs were infused with 5 per cent glucose in saline.

The right coronary artery was dissected from approximately 10 mm. distal to its origin in the aorta to the main bifurcation of the right ramus marginalis acuti and the ramus circumflexus dexter. The smaller branches leaving this area were ligated and severed. This procedure permits 10 to 20 mm. of the artery to be completely loosened from the fatty auriculo-ventricular groove. The artery was ligated and the time noted. A hole was cut distal to the ligature and a tube of polyethylene or nylon was inserted and doubly ligated with 3-0 silk. Two types of tubing were alternately used: (1) polyethylene (Intramedic†) and (2) nylon.‡ The diameter of the tube was selected so that the inner diameter would be as close to the original vessel inner diameter as possible. Sizes from 0.97 mm. to 2.43 mm. (external diameter) were used. The tube was filled by blood from the distal part of the artery by the reverse flow. In the first series of operations a small piece (15 to 20 mm.) of the tube was threaded directly into another hole cut proximal to the ligature (Fig. 1, *A*). In the second series, the tube (120 to 140 mm.) was formed into a loop with an approximate inner diameter of 15 to 25 mm. and the other end threaded into the proximal hole. Also, the proximal part of the tube was secured in the artery by 3-0 silk (Fig. 1, *B*). In a third series of dogs the internal mammary artery was dissected to 10 to 15 mm. from its origin and divided so that a 30 to 40 mm. free proximal stump was obtained. The artery was then transposed to the mediastinal side of the pleural cavity and secured with 3-0 silk stitches. A nylon or polyethylene tube (130 to 150 mm.), filled with heparinized saline, was inserted into this stump and secured with two or three 3-0 silk stitches. The distal end of the

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*E. R. Squibb & Sons, New York, N. Y.
†Clay Adams Company, Inc., New York, N. Y.
‡Thermoglas Inc., Gothenburg, Sweden.

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[illegible] In [illegible] the [illegible] cannot be excluded. Thus, in [illegible] by [illegible] in d by autopsy [illegible] the tube remained open [illegible]

[illegible] Using the loop technique, 10 dogs were operated upon [illegible] survived. One dog died on the [illegible] succumbed during the first postoperative [illegible] In 5 dogs, sacrificed after 4 to 6 weeks, the tube was [illegible] in one case.

[illegible] *Internal Mammary Artery and Coronary Artery.*— [illegible] with anastomosis between the right internal [illegible]

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mammary artery and the right coronary artery. Nylon tubes and polyethylene tubes were used alternately. All dogs survived the operation. Two dogs are still alive, and we intend to keep them alive as long as possible to find out the fate of the anastomosis after long time survival. One dog died on the eighth postoperative day from pleural empyema, in this animal the polyethylene tube was found to be patent and there were no signs of myocardial infarction. Seven dogs were killed 6 to 8 weeks after the operation. In none of these dogs were there any signs of infarction. In 3 of the dogs, however, there was complete or partial obstruction of the tube, whereas the distal part of the coronary artery was patent. In all 3 cases this happened in relatively small dogs in which a small caliber tube was used.

Six dogs died during the first week after operation, usually on the fourth or fifth postoperative day. In all of these cases the death was due to hemorrhage caused by slipping of the tube, either from the coronary artery (4 cases) or from the internal mammary artery (2 cases). Polyethylene tubing was used in all of these cases. In none of these dogs were there signs of infarction and, except for post mortal clotting, the tubes were found to be patent in all but one case, in which thrombosis could not be excluded.

Ventricular fibrillation or cardiac arrhythmia of any kind did not occur during this kind of procedure.

Summing up, in 48 dogs operated upon with insertion of plastic tubes in the coronary artery, there was proof that the tubes remained open after 4 weeks in 16 out of 24 survivors (67 per cent). Since a number of dogs are still living (3 to 18 months after operation), this percentage may be altered as the dogs are re-examined at various intervals.

DISCUSSION

Operative Technique.—The insertion of a small piece of tubing of an inert material in a small coronary artery is a difficult procedure. Once the one end of the tube has been secured in the distal part of the artery, the stiffness of the tube in connection with the movements of the heart makes it a difficult task to insert it in the proximal part of the artery without kinking, or the tube slipping out from the already inserted end. In the beginning, these experiments, in regard to the time used for this part of the operative procedure, took more than 5 minutes as a rule, which is a long time for total occlusion of one of the major coronary arteries and carrying a considerable risk of irreversible ventricular fibrillation. The mean total occlusion time for this procedure in all experiments was 5.3 minutes.

The loop technique was technically much easier to handle. With the freedom of movement provided by the longer loop, the above mentioned difficulties were partly overcome. This is also demonstrated by the period of occlusion which, with the loop technique, averages 3.7 minutes. Still better and easier is the use of a connection from the internal mammary artery. This could be achieved with less than one minute of occlusion. In the last two series, no dog died during the operation and there were no alterations in the heart rhythm as judged from direct observation of the heart and a monitoring electrocardiogram.

Two kinds of synthetic material were used in this investigation; nylon and polyethylene tubing. Comparing the two fabrics used by us, the nylon tubing is somewhat more rigid than polyethylene and it is easier to thread into a hole cut in a small vessel. On the other hand, it is more difficult to bend, and we had more trouble inserting it in the proximal hole after the piece of tubing had been secured in the hole distal to the ligature than we had when polyethylene tubing was used. The wall of the nylon tube used by us is thinner than that of the polyethylene tube, permitting a somewhat larger flow with a tube of the same outside diameter. In the long run there were no differences between the two materials since both remained open in a fair number of cases and both apparently provided sufficient blood flow to the myocardium.

In the beginning of these experiments, the tubes were siliconized or saturated with heparin solution. This did not, however, contribute to survival or to a longer period of flow through the tubes, and was later abandoned. This observation is in agreement with that of Donovan[4] who observed that lining with silicone or the use of heparin in polyethylene tubes inserted in the femoral arteries did not increase the average duration of patency. This is also the reason why we did not keep these dogs on anticoagulants during the postoperative period.

Ventricular Fibrillation.—Ventricular fibrillation is a well-known complication after sudden occlusion of a major coronary artery.[2, 14, 15, 19] Since we[8] had good experience with the antifibrillatory properties of procaine amide in another field of cardiac surgery with high fibrillation incidence (namely, open cardiac surgery in hypothermia with venous inflow occlusion), we used this drug in some experiments hoping that in this field also, it should be valuable as a protecting agent. Half of the dogs in the "direct" series received procaine amide as an intravenous infusion during the operation, whereas the other half of the animals were infused with glucose in saline. There was, however, no significant difference in the incidence of fibrillation in these two groups. Thus, it seems that addition of procaine amide to the intravenous fluid drip does not diminish the risk of operating upon the coronary arteries in normothermia.

Fibrillation most often occurred within 30 seconds after the release of the blood flow from the proximal part of the coronary artery. This is a well-known phenomenon.[1, 22] Ventricular fibrillation also was reported shortly after the release of the blood flow to hypothermic hearts after complete inflow occlusion.[21] Sewell, Koth, and Huggins[18] found, after temporary occlusion of the anterior descending coronary artery of the dog, that sudden return of the arterial flow caused ventricular fibrillation in 6 of 31 animals, whereas there were no fatalities if they made the release of the flow intermittently. In the beginning of our experiments, we were not aware of Sewell's and his associates' observations and the release of the flow through the plastic graft was done as quickly as possible in order to diminish the time of coronary occlusion. Later, we were careful to release the blood flow very slowly and, although the number of experiments do not permit statistical analysis, we have the impression that this procedure was helpful in avoiding ventricular fibrillation. Only one dog fibrillated during an operation using the slow release of coronary blood flow.

Survival of the Dogs.—In a series of experiments reported earlier, a sham operation on the right coronary artery was done including ligation of the artery, but with no attempt to insert any kind of artificial blood supply to the myocardium distal to the ligature. The mortality with this procedure during the operation and in the immediate postoperative period was 93 per cent. In the three series of dogs, presented in this paper, in which the ligated area in the right coronary artery was bypassed by an artificial graft, the mortality rate was considerably lower, 45 per cent with the "direct" method, 30 per cent with the "loop" method, and 43 per cent using the mammary artery anastomosis. These figures represent the total mortality rate, including technical errors and apparently irrelevant postoperative complications. From these data it is apparent that the plastic tubes, bypassing the ligated part of the coronary artery, contribute to the survival of the animal.

Patency of the Tubes.—Tubes of plastic materials, implanted in small vessels, usually become obliterated by thrombosis very soon. In another series of experiments,[9] we found this also to be true when we inserted tubes of the same size and material as were used in the heart in peripheral systemic arteries. Why, then, do nylon and polyethylene tubes inserted in the coronary artery remain open in so surprisingly high a per cent of the cases? Some explanations may be discussed. The flow in the coronary arteries is faster than in the other arteries of the body. The venous outflow from the coronary system is very efficient due to a network of anastomosing venous channels. A third factor would be that the tubes move with the movements of the heart, causing a constant shaking of the tubes. In these cases, where the tubes were inserted into the distal part of the coronary artery, the squeezing power of the myocardium can hardly be taken into consideration; this, however, would possibly be the case if the tubes had been implanted directly in the myocardium. Sabiston and Fauteux[16, 17] discuss this possibility as the reason why implants of the carotid artery into the right or left myocardium of dogs remained open in a fair number of cases.

Assuming that the chemical composition of the plastic tube itself would have an effect on the clotting of the blood, it would be reasonable to assume that the length and caliber of the tube (*namely, the exposed surface of plastic material*) would influence the tendency of clotting. Since the elasticity of the tube is less than that of an artery, this would also affect the blood flow, presumably with an increased risk of intravascular clotting parallel to an increase of the length of the tube. The material presented in this paper does not, however, permit any conclusions in this respect.

A last contributory factor could be the anastomosis technique. If an anastomosis between two arteries is accomplished with sutures of any kind, there will almost always be some intimal lesions at the sut [illegible] possible focus for the formation of a thrombus. With the technique used in these dogs, the plastic tube is pushed into a vessel with the intima intact at the place where the end of the tube is secured.

Further experiments with plastic tubes supplying portions of the myocardium are in progress and will be reported separately.

SUMMARY

A technique is described in which nylon or polyethylene tubes were used as artificial grafts, either bridging an occluded part of the right coronary artery or as an anastomosis between the internal mammary artery and the coronary artery distal to a ligature. In 24 dogs, surviving more than 4 weeks (longest period of observation—18 months), the tubes were found to be patent in 16 cases. Some technical points as well as some possible reasons for the patency of the tubes in the coronary artery system are discussed.

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STUDIES OF THE CORONARY CIRCULATION

III. Intramyocardial Implantation of Nylon Tubes After Ligation of a Major Coronary Artery

Knut Haeger, M.D., Malmö, Sweden, and Georg R. Wallgren, M.D.,**Helsingfors, Finland*

In 1946, Vineberg[1] reported the successful implantation of the left internal mammary artery in the left internal mammary artery in the left myocardium of the dog. Later, it was demonstrated that a collateral circulation developed between the implanted artery and the left descending coronary artery.[2] Some years ago, Vineberg and his associates[3] reported on 4 years of clinical experience with the method; 70 per cent of their patients were reported to be markedly improved after the procedure and were able to return to work.

As was also observed by the originators of the method, significant anastomosis did not develop in all cases, and the lumen of the implanted artery very often was found to be obliterated by endarteritic changes and by thrombi formation.[4, 5, 6] Bakst and his co-workers[6] were unable to find that the implanted artery contributed to the intercoronary anastomotic flow. Many attempts have also been made to modify and improve Vineberg's original method. Julian and his co-workers[7] created fistulas between the internal mammary artery and the mammary vein, and implanted these in the myocardium. They reported that the vast majority of these fistulas closed, but that some remained open a long period of time. Carey and associates,[8] in a two-stage operation, used the internal mammary artery as a bridge between the left atrium and the myocardium, and demonstrated that this procedure afforded a certain degree of protection against ventricular fibrillation or infarction which generally develops following ligation of the descending branch of the left coronary artery. The same group of workers[9] compared the effects of implantation of the subclavian and the internal mammary arteries in the myocardium and found some evidence that the use of the bigger subclavian artery appeared to offer greater protection against infarction and this artery seemed to be less exposed to endarteritic occlusion.

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*Halsted Fellow at the University of Colorado School of Medicine, Denver, Colo., 1957-1958, from the Department of Experimental Surgery, Allmänna Sjukhuset, Malmö, Sweden.

**Foreign Exchange Student of the Institute of International Education, 1957-1958, from Helsingfors, Finland.

In 12 dogs, Sabiston and Fauteux[10] created an anastomosis between the carotid artery and the right myocardium. Three of the dogs died of ventricular fibrillation, in the remaining 9 dogs, however, the implanted artery was found to be patent in 6 cases and thrombosed in 3. When the left carotid artery was implanted in the left myocardium, the vessel was found to be grossly patent in 28 out of 32 animals. The time of observation varied between 22 and 246 days.[11] Smith and coworkers[12] connected the aorta with the left myocardium by means of a vessel graft or a nylon tube, and demonstrated the graft to be open in the dog after one year. In 2 human patients they used a venous graft and a nylon tube, respectively, and reported excellent postoperative results in both cases. Finally, Massimo and Boffi[1] created a canal between the left ventricular cavity and the left myocardium by means of a nylon T tube (4.5 mm in diameter) and reported good results in the experimental animals.

It seems that one of the major problems using the Vineberg approach, or its modifications, is the impending risk of intimal proliferation and subsequent thrombosis of the supplying artery. We have found polyethylene or nylon tubes remain open in a high percentage of dogs when the tubes are inserted in the coronary artery. Therefore we decided to use similar tubes as a bridge between the internal mammary artery and the ischemic myocardium.

METHODS

Mongrel dogs weighing between 7 and 20 Kg. were anesthetized with 30 to 40 mg. per Kg. Nembutal intravenously. After intubation, the respiration was artificially maintained with 100 per cent oxygen. After thoracotomy in the lateral position, the internal mammary artery was dissected to 10 to 15 mm. from its origin, and was divided so a 30 to 40 mm. free proximal stump was obtained. Then the artery was transposed to the mediastinal side of the pleural cavity by means of some 5-0 silk stitches. A nylon tube* (outer diameter, 1.57 to 2.80 mm.) was inserted into the arterial stump and secured by two or three 3-0 silk ligatures. The other end of the tube, which previously had been perforated with a hot needle in several places, was attached to a silk ligature. Using a slightly curved or straight needle, this end was buried subendocardially in the myocardium parallel to one of the major coronary arteries (Fig. 1). In some cases, the distal end of the tube could simply be pushed into place through a small epicardial incision. If any bleeding occurred at the ends of the buried part of the tube, the hole was closed with atraumatic 5-0 silk, sometimes tied over a small piece of Gelfoam.

Finally, the selected coronary artery was ligated and the blood flow from the mammary artery via the tube was released. In some instances, a small hematoma developed around the buried tube. In the last dogs operated upon the myocardial end of the tube was closed so the blood could only leave it through the small needle stick holes. The bridging part of the tube was secured to convenient tissues such as the auricular wall, the pericardium, or on individuals with previous impairment of the coronary flow, remains to be investigated. Preliminary results in dogs operated upon with this technique after artificially induced coronary thrombosis and subsequent myocardial infarction do not, however, indicate a significant increase in the incidence of ventricular fibrillation.[15]

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*Thermoglas Inc., Gothenburg, Sweden.

Protection Against Death Following Coronary Artery Ligation.—The experimental evaluation of a method for supplying arterial blood to the heart is very difficult since the results of the irritation caused by the pericardiotomy alone seem to offer a certain degree of protection.[16] As pointed out by Garamella and associates[17] and, indirectly, by Milch and his associates[18] control experiments from other laboratories cannot be relied upon due to the numerous variables of acute ligation of a major coronary artery. This is also very clear from the varying results of acute coronary ligation as they have been reported by numerous investigators. For an adequate comparison, the animals of the control series should be treated exactly as those of the experimental series, and the ligation of the coronary artery in the former should be done with the same operative trauma as in the procedure under investigation. In other words, the ligation of the coronary artery in the control series should be made as a sham-operation simulating the operative technique of the procedure under investigation.

Such sham operations on the right coronary artery were made in this laboratory with an immediate postoperative death of 93 per cent. After high ligation of the left descending coronary artery (the septal branch not included), the mortality in 7 dogs was 100 per cent. In the latter series, the septal branch was not included; the observance of this detail is of importance.[19] The mortality following unilateral intramyocardial implantation of nylon tubes and simultaneous corresponding ligation of a major coronary artery was 2 out of 12 dogs in this series. Consequently, it appears the implantation of the nylon tube added to the protection of the heart.

The Patency of the Tubes.—Apparently nylon tubes implanted into the myocardium remain open for some time but later, probably after about 6 weeks, become occluded by thrombosis. On the other hand, when similar tubes were used in an identical manner in various parts of the systemic circulation, they usually became obstructed very early. In some instances, there was proof of obstruction at the second to the fifth day after operation.

Six weeks is an astonishingly long time. Nevertheless, it is considerably shorter than when tubes of the same caliber were inserted directly in the coronary vessels. In earlier experiments, in which this technique was used, we have seen such tubes occasionally remain patent more than one year.[11, 20] At the present time, we are satisfied that the intramyocardially implanted tubes remain open long enough to supply the myocardium with oxygenated blood during the critical phase after ligation of a coronary artery. This critical period is the time during which the normally resting intra- and extracoronary anastomoses need to develop as functional units, a period which in the dog is stated to be between 4 and 12 days after the ligation.[21]

There seems to be some fundamental difference between the tendency to clot in a tube of inert material inserted into a peripheral artery and a coronary artery, respectively. It is to be remembered though that morphologically as well as physiologically there is a marked dissimilarity between the vascular supply to the heart and that of any other organ or part of the body.

First, the blood vessels in the myocardium are embedded in a tissue the syncytial structure of which is not similar to any elsewhere in the body. Furthermore, there is no organ that is so well supplied with afferent as well as efferent blood vessels as the myocardium. The amount of capillaries in the adult human myocardium is calculated to be between 3,000 and 4,000 per square millimeter, as compared with less than 2,000 capillaries per square millimeter in the skeletal muscle. In the normal adult heart every single fiber is supplied by its own capillary, which also is an unique arrangement.[72]

There is now a general agreement that the coronary arteries are end arteries in the physiologic sense, i.e., one artery branches within the region where it runs and supplies this and no other area. From the anatomic point of view, however, they are not end arteries since there is a richly developed system of interarterial anastomoses at different levels throughout the length of the artery. It is believed that during normal conditions at least most of these communications are closed. After injection of fluids of high viscosity, too thick to penetrate the capillaries, these anastomoses were found to be of considerable size, but *it was a rare finding to have one coronary artery filled* with the material injected into another.[73, 74] Given enough time, the interarterial anastomoses open up after some kind of stimulation, as for instance if a pressure gradient develops between two arteries,[75] or if the biochemical milieu in the heart in some way is altered, as for instance by tissue hypoxia.[76] This is an important difference between the coronary system and, for example, the arteries of an extremity. Another dissimilarity that may be important as regards the clotting mechanisms is the spontaneous rhythmical movements of the coronary arteries as reported by Rothlin[77] and Hausler and Filippi.[78]

The smooth muscles in the walls of the coronary arteries are arranged somewhat differently from those in a peripheral artery. In the proximal part of a coronary artery near the aortic ostium and also, in the distal parts of the artery near the apex of the heart, the smooth muscle fibers are arranged as a spiral. The purpose of this arrangement is not clearly understood, probably it serves as some kind of protective mechanism to ensure coronary flow throughout the cardiac cycle. A similar mechanism has been reported in the cardiac veins.[79] The walls of these veins contain more smooth muscle, comparatively, than other veins; especially, the longitudinal layer of muscles in the cardiac veins are very well developed. This permits the veins to exert an active resistance to the pressure of the surrounding myocardial muscle and thus, the venous outflow from the myocardium is secured even under myocardial systole. The topographical arrangement of the cardiac veins in several different and independent systems also provides on individuals with previous impairment of the coronary flow, remains to be investigated. Preliminary results in dogs operated upon with this technique after artificially induced coronary thrombosis and subsequent myocardial infarction do not, however, indicate a significant increase in the incidence of ventricular fibrillation.[15]

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Six weeks is an astonishingly long time. Nevertheless, it is considerably shorter than when tubes of the same caliber were inserted directly in the coronary vessels. In earlier experiments, in which this technique was used, we have seen such tubes occasionally remain patent more than one year.[14, 20] At the present time, we are satisfied that the intramyocardially implanted tubes remain open long enough to supply the myocardium with oxygenated blood during the critical phase after ligation of a coronary artery. This critical period is the time during which the normally resting intra- and extracoronary anastomoses need to develop as functional units, a period which in the dog is stated to be between 4 and 12 days after the ligation.[21]

There seems to be some fundamental difference between the tendency to clot in a tube of inert material inserted into a peripheral artery and a coronary artery, respectively. It is to be remembered though that morphologically, as well as physiologically, there is a marked dissimilarity between the vascular supply to the heart and that of any other organ or part of the body.

First, the blood vessels in the myocardium are embedded in a tissue, the syncytial structure of which is not similar to any elsewhere in the body. Furthermore, there is no organ that is so well supplied with afferent as well as efferent blood vessels as the myocardium. The amount of capillaries in the adult human myocardium is calculated to be between 3,000 and 4,000 per square millimeter, as compared with less than 2,000 capillaries per square millimeter in the skeletal muscle. In the normal adult heart every single fiber is supplied by its own capillary which also is an unique arrangement.[72]

There is now a general agreement that the coronary arteries are end arteries in the physiologic sense, i.e., one artery branches within the region where it runs and supplies this and no other area. From the anatomic point of view, however, they are not end arteries since there is a richly developed system of interarterial anastomoses at different levels throughout the length of the artery. It is believed that during normal conditions at least most of these communications are closed. After injection of fluids of high viscosity too thick to penetrate the capillaries these anastomoses were found to be of considerable size, but it was a rare finding to have one coronary artery fill with the material injected into another.[73, 74] Given enough time, the interarterial anastomoses open up after some kind of stimulation as for instance if a pressure gradient develops between two arteries,[75] or if the biochemical milieu in the heart in some way is altered as for instance by tissue hypoxia. This is an important difference between the coronary system and, for example, the arteries of an extremity. Another dissimilarity that may be important as regards the clotting mechanisms is the spontaneous rhythmical movements of the coronary arteries as reported by Rothlin[77] and Haasler and Filippi.[78]

The smooth muscles in the walls of the coronary arteries are arranged somewhat differently from those in a peripheral artery. In the proximal part of a coronary artery near the aortic ostium and also in the distal parts of the artery near the apex of the heart the smooth muscle fibers are arranged as a spiral. The purpose of this arrangement is not clearly understood; probably it serves as some kind of protective mechanism to ensure coronary flow throughout the cardiac cycle. A similar mechanism has been reported in the cardiac veins.[79] The walls of these veins contain more smooth muscle, comparatively, than other veins, especially the longitudinal layer of muscles in the cardiac veins are very well developed. This permits the veins to exert an active resistance to the pressure of the surrounding myocardial muscle and thus, the venous outflow from the myocardium is secured even under myocardial systole. The topographical arrangement of the cardiac veins in several different and independent systems also provides excellent facilities for drainage of blood from the myocardium. In our experiments, little or no hematoma developed around the perforated end of the tube after its implantation into the myocardial muscle, whereas large hematoma immediately developed around the same kind of tube inserted in a skeletal muscle or in a parenchymatous organ. The very effective venous drainage system probably is responsible for this difference. It is well known that stasis is a predisposing factor for intravascular clotting, and it might be that these effective drainage facilities prevent stasis around the tube and indirectly permits a steady flow through the tube. In the papers by Sabiston and Fauteux,[10, 11] there are some observations which support this hypothesis. They implanted the carotid artery in the right ventricular wall and observed a flow of between 1.6 and 3.2 c.c. per minute in the graft in some of their animals. If, however, the conditions of draining were improved by partial communication of the graft with the cavity of the heart, the amount of flow through the implanted artery increased tenfold or more. This may be taken as evidence of the significance of good drainage to the flow in the afferent part of the system. In our series we did not deliberately attempt to drain the tubes partially to the ventricular cavities. It is possible it would be wise to do so in the future.

The vasomotor innervation of the coronary arteries "is unsurpassed by any other artery in the body."[30] Both divisions of the autonomic nervous system are represented. It is now held that, contrary, to the systemic arteries, the parasympathetic nerves carry the vasoconstrictor fibers and the sympathetic nerves the vasodilator fibers. According to Poiseuille's law, even very little diminution of the cross surface of an artery influences the flow considerably. This has also been experimentally demonstrated by Mann and associates.[31] Since there is a difference in the vasoconstriction innervation of the coronary system and the peripheral system, it might be that vasoconstriction occurs to a lesser degree in the former arteries and, thus, the chances of impairment of blood flow are less pronounced.

In the dog, the mean heart weight is about 0.75 to 1.0 per cent of the total body weight.[32] This comparatively small fraction of the total weight of the animal is, however, supplied by no less than 4 to 5 per cent of the total cardiac output; in emergencies it can rise as high as 14 per cent.[33] This means that the flow in the coronary arteries, even under resting conditions, is very high, and definitely higher than in the systemic arteries. Assuming the total coronary inflow in the normal resting dog averages about 70 c.c. per 100 gram left heart per minute,[33] the flow through the coronary artery will be just a little more than 1 c.c. per second. In a coronary artery with an internal diameter of 2 mm. this means that the velocity of the blood stream will be about 30 cm. per second. The velocity of the blood stream through the aorta has been theoretically calculated to be about 22 cm. per second,[34] and, experimentally, values about 18 cm. per second have been reported.[35] When the aorta branches in smaller arteries, the combined cross section areas of these increase and the velocity decreases. In the peripheral extremity arteries, velocity figures of about 10 to 20 cm. per second are reported.[36]

Thus, the velocity of the blood stream through the coronary arteries is at least two times faster than that of peripheral arteries of corresponding size. Also, this fact may add to the lesser tendency of intravascular blood clotting in tubes connected with the coronary system. Of course, this factor is irrelevant when the nylon tubes are implanted directly in the myocardium, but certainly it may have some bearing when pieces of tubes are used as a bypass and inserted as a bridge between two severed parts of a coronary artery.

Also, in other respects, the dynamics of blood flow are different in the coronary arteries and in the peripheral arterial system. A comparison of the interrelations of pressure, vascular volume, and flow in the coronary artery and, for example, in the femoral artery, reveals some interesting points. In the peripheral artery there is a rapid increase in flow at the onset of systole. This increase reaches its peak shortly before the arterial pressure starts to fall, and then begins to diminish rapidly. As the vascular volume is increased, there is a retardation of the flow and for a moment there is a short period when the flow not only is decreased, but even reversed. Wright and Phelps[37] showed this was true in the arteries of the extremities and in the common carotid arteries, whereas there was no evidence of reversal of flow in the renal, hepatic, and superior mesenteric arteries.

In the coronary arteries, on the other hand, the pattern of the flow curve is different. As was demonstrated by Gregg and Green,[38] in the dog there is a very short period of backflow also in the coronary arteries at the onset of the phase of isometric contraction in the myocardial muscle. This period, however, is considerably shorter than the backflow phase of the peripheral arteries. In the coronary arteries, it lasts about 1/20 of the total cardiac cycle, whereas it is little more than two times that length in the peripheral system.[37, 38, 39] The amount of blood that is rejected during the backflow phase is negligible in the coronary arteries. It amounts to about 0.006 ml. per heartbeat in the dog as compared with a total flow of about 0.2 ml. per heartbeat during the whole cycle. As in the peripheral arteries, there is also a diminution of flow with falling aortic pressure, but in the coronary arteries the flow never reaches the zero line in this phase and, during diastole it quickly rises again after the closure of the aortic cusps.

It is difficult to say whether these hemodynamic differences may play a role for the tendency of clotting and thus explain why tubes inserted in the coronary system remain open for a longer time than tubes in the systemic arteries. Although it is well established that stasis is an important factor in the pathogenesis of thrombosis, we have no evidence that a small relative difference of, for instance, the duration of the backflow phase in two arterial systems may influence the intravascular clotting propensity. For the moment we only want to stress that important dissimilarities do exist between the coronary and the systemic circulation, and that one or more of these differences may account for the varying results obtained after insertion of nylon tubes in the coronary system and the peripheral system, respectively.

In the present studies we have used a nonsuture technique at the insertion of the tubes. In an earlier paper from this laboratory,[11] it was discussed whether this might have added to the sustained patency of the tubes. It was demonstrated by Blakemore and Lord[10] and by Egdahl and Hume[41] that the nonsuture method may be effectively used in small arteries. In the present series, however, in which the nonsuture technique was used in both peripheral vessels and in arteries inserted into various parenchymatous organs on one hand, and in tubes inserted into the myocardium or into the coronary arteries themselves on the other, there was a marked difference in the frequency of thrombosis. This probably means that the nonsuture technique per se is not responsible for the favorable results observed when the tubes were inserted in the heart.

An alternative explanation could be offered if the clotting mechanism were inhibited by some local factor in the myocardium or modified by some alterations caused by changes in the heart metabolism after infarction. Some pilot experiments to clarify this problem were undertaken in this laboratory. As yet, however, no certain evidence of such a mechanism has been established. Some observations reported in the literature are, however, of interest. Tietze and Schulz[42] reported an increased fibrinolytic activity in plasma following myocardial infarction in man; Tagnon and co-workers[43] observed fibrinolysis during hemorrhagic shock, and Kwaan and McFadzean[44] demonstrated the appearance of a fibrinolytic substance in the blood running through an extremity temporarily deprived of its arterial supply. These observations support the concept of a decreased tendency of intravascular clotting in an ischemic area. On the other hand, Hume[45] observed a depression of the fibrinolytic activity in patients with myocardial infarction during the first 8 days after the onset of the disease. Thus, the reports in this field are controversial, and for the moment nothing can be said of the role of the biochemical factors in the clotting mechanism as applied to the patency of artificial tubes inserted in the myocardium.

SUMMARY

Nylon tubes were inserted into the internal mammary artery in the dog and the other perforated end of the tube was embedded in the myocardium close to one of the major coronary arteries. The pertinent artery was subsequently ligated and the results of this operation were compared to control experiments without implantation of tubes.

The mortality after acute ligation of the right coronary artery in the dog was, under the conditions of these experiments, 93 per cent, and ligation of the left descending coronary artery, 100 per cent. After implantation of tubes, 10 dogs out of 12 survived. The tubes were usually found to be patent if the

dog was sacrificed within 6 weeks, otherwise the tubes were found to be obstructed by thrombosis. Six dogs out of 7 survived bilateral coronary ligation after tube implantation in two stages.

When the tubes were inserted in peripheral arteries and either embedded in parenchymatous organs or skeletal muscle or were inserted in the peripheral stump of the same artery, there was early thrombosis in 18 out of 20 experiments.

When a tube was inserted in the myocardium and the pertinent coronary artery ligated and the tube later was clamped the dog did not survive if the clamping was done within 5 days after the original operation.

It is felt the implantation of nylon tubes supplying the ischemic myocardium with arterial blood from the internal mammary artery adds to the protection of the heart from death of myocardial infarction. The possible reasons for the prolonged patency of the tubes implanted in the heart are discussed.

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STUDIES OF THE CORONARY CIRCULATION

IV. Surgical Treatment of Acute Experimental Myocardial Infarction in the Dog

Knut Haeger, M.D., Malmö, Sweden, and Georg R. Wallgren, M.D.,** Helsingfors, Finland*

Contrary to the case of acute occlusion of a peripheral artery, the acute occlusion of a coronary artery generally has been considered a subject of non-surgical treatment. However, as early as 1947, Gordon Murray[1] predicted that "the day may come when the best plan of dealing with a coronary thrombosis would be an emergency operation." He supported this view with experiments on dogs, in which the ballooning area occurring after myocardial infarction was excised. He noted this procedure of reducing the paradoxical systole of the infarcted area not only increased the rate of survival but also markedly improved the cardiac output and increased the blood pressure Cardiostatorrhaphy, as described by Allen,[2] also attempts to prevent or diminish the area of ballooning. This author stated that the heart became more efficient after this procedure of stabilization and compression of the ischemic area.

Temesvári[3] created myocardial infarction by acute ligation of the right coronary artery in dogs. Twelve to 48 hours later he excised the ischemic area and covered the defect with a pedicled flap of the diaphragm or the pectoral muscle. Detailed information of the rate of survival in these dogs as compared with untreated animals is not given in this paper. It is, however, stated that some of the dogs survived the operation by 8 to 10 months. At autopsy, the flaps were found to be subjected to fibrous degeneration and, in some cases, even to the formation of cartilaginous tissue. Also, Forcheri and Castellani[4] excised the ischemic part of the myocardium after ligature of the middle third and the left anterior coronary artery. Although these authors observed the cicatrization was more certain and stronger following resection of the infarcted area, they recommend the procedure only in selected cases, due to the high operative mortality.

As far as we know, the above-mentioned procedures are the only attempts of surgical intervention in acute myocardial infarction in experimental animals.

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*Halsted Fellow at the University of Colorado School of Medicine, Denver, Colo., from the Department of Experimental Surgery, Allmänna Sjukhuset, Malmö, Sweden.

**Foreign Exchange Student of the Institute of International Education from Helsingfors, Finland.

Until recently, it has been difficult to produce slow coronary occlusion resembling the conditions in man. In 1956, however, Gage, Olson, and Chardack[5] reported on a simple and ingenious method to create coronary thrombosis and subsequent myocardial infarction in the dog. The insertion of a magnesium-aluminum alloy needle in one of the major coronary arteries makes it possible, in the dog, to produce a slowly developing coronary thrombosis, causing clinical and electrocardiographic evidence of myocardial ischemia.

In earlier experiments in this laboratory,[6] we found that dogs survived acute ligation of one of the major coronary arteries if a nylon tube was inserted in the internal mammary artery and embedded in the myocardium. In those experiments, the tube was implanted in healthy myocardium and the occlusion of the pertinent coronary artery was not made until the extracardial arterial blood supply had been established through the tube. Since we found these tubes mostly remained patent, at least for some weeks, it occurred to us a modification of this procedure might be useful in the treatment of acute myocardial infarction. It is the purpose of this paper to report the results of intramyocardial implantation of a nylon tube at a time when myocardial ischemia was present.

METHODS

For the experiments, adult healthy mongrel dogs of both sexes, weighing 10 to 25 Kg., were used. The dogs were anesthetized with intravenous Nembutal (30 to 40 mg. per kilogram of body weight) and intubated. Artificially controlled respiration using 100 per cent oxygen was maintained throughout the operation and continued for some hours postoperatively.

The right or left side of the heart was alternatively exposed by a thoracotomy in the fourth or fifth interspace in the lateral position. The pericardium was opened and the chosen coronary artery carefully dissected. An 18 to 23 mm. piece of a magnesium-aluminum alloy wire* was inserted into the lumen of the artery. The technique is described in detail by Gage and his co-workers.[5] In the right coronary artery, the wire was placed just proximal to the main bifurcation; in the left descending artery, as near the main bifurcation as possible without interference with the septal artery; and, in the left circumflex artery, just distal to the main bifurcation of the left common coronary artery. Minor aberrations from these sites could not be avoided in some animals. Thus, in one case the septal artery was blocked, which resulted in infarction of the interventricular septum and subsequent damage to the conductive system.

After insertion of the wire, the pericardium was closed, the lung expanded, and the chest was closed with suction drainage. Electrocardiograms were recorded before and after the operation, and repeatedly during the postoperative course. The electrocardiographic observations will be subjected to a detailed analysis and published separately.[7]

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*Magnesium (98%) and aluminum (2%). We are indebted to the Denver Branch of the Aluminum Company of America for a generous supply of this alloy.

Sixteen dogs were treated only with the described procedure and were kept as controls. Postmortem examination was made in all cases and evidence of coronary thrombosis and myocardial infarction was noted.

Another 15 dogs were observed clinically and with repeated electrocardiograms on the days following the insertion of the wire. When electrocardiographic signs of myocardial ischemia were present, and/or the condition of the dog became alarming, it was reoperated upon. The previous skin incision was opened and the thorax was entered through the same or an adjacent interspace. A nylon tube* (external diameter 2.4 to 2.8 mm.) was inserted into the internal mammary artery as described in an earlier paper.[7] A purse-string 3-0 silk suture was placed in the myocardium close to the ischemic area and a 1 to 2 mm. incision was made in the epicardium. It was noted that if the suture was placed inside the bluish, sometimes bulging, ischemic area, it very easily cut through the muscle fibers and had to be replaced in an intact area.

The distal end of the tube that was perforated was filled with blood from the mammary artery and pushed through the epicardial incision. The purse-string suture was tightened around it and tied over a small piece of Gelfoam. An attempt was made to place the intramyocardial part of the perforated tube at the borderline between the healthy and the ischemic parts of the myocardium. After release of the blood flow through the tube, there usually was no, or very little, bleeding backward from the epicardial incision. The tube was secured to convenient tissues by some silk stitches. Special care was taken that the tube did not create a possibility for herniation of the lung.

In 6 dogs the same operation was undertaken on the same indications as above, but in these cases the nylon tube was closed and thus, a sham operation was performed without any blood entering the myocardium from the internal mammary artery.

Since it is known that adhesions may form between the pericardium and the epicardium,[8] rendering additional myocardial blood supply, the pericardial incision was closed only at the base of the heart to cover the tube. The chest was closed with drainage. The dog was kept on artificial respiration with 100 per cent oxygen one to 2 hours postoperatively, and 500,000 I.U. of penicillin was given intramuscularly. Electrocardiograms were recorded before the operation and during the postoperative course.

RESULTS

The 16 dogs which were only subjected to Mg-Al wire implantation died within 15 days of the operation (Table I). However, 4 dogs fibrillated during or immediately after the operative procedure. These deaths must be a sequel of the manipulations of the coronary artery or caused by mechanical occlusion by the wire per se.

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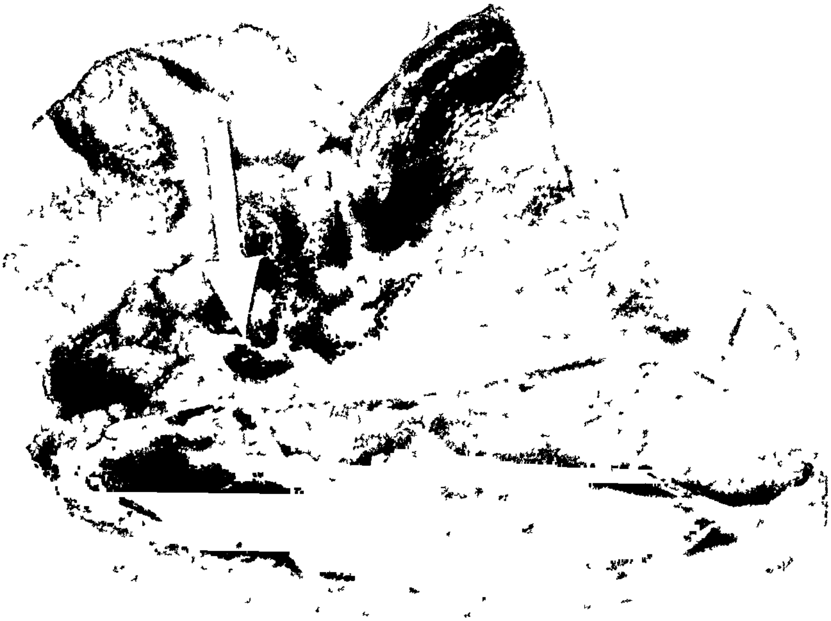
*Thermoglas Inc., Gothenburg, Sweden.

At postmortem examination of the remaining dogs, myocardial infarction was observed in all cases. In 4 dogs, surviving 4 to 15 days after the wire implantation, the wire was dissolved and a thrombus was found at the site of the implantation (Fig. 1). In some other cases there was slight erosion on the surface of the wire, and there were signs of beginning thrombus formation (fibrin deposits, etc.).



ig 1.—*Thrombus attached to the wall (at arrow) of the right coronary artery 7 days after the insertion of a magnesium-aluminum alloy wire*

TABLE I. CONTROL EXPERIMENTS

EXPERIMENT NO.	SITE OF Mg-Al WIRE IMPLANTATION	DEATH (TIME AFTER IMPLANTATION)	NOTES
1	Right coronary artery	1 hour	Ventricular fibrillation
2	Right coronary artery	4 hours	Severe myocardial ischemia
3	Right coronary artery	4 days	Severe myocardial infarction
4	Right coronary artery	7 days	Artery occluded by thrombus, myocardial infarction (Fig. 1)
5	Right coronary artery	8 days	Artery occluded by thrombus, myocardial infarction (Fig. 1)
6	Right coronary artery	15 days	Artery occluded by thrombus, myocardial infarction (Fig. 1)
7	Left descending artery	Immediately	Ventricular fibrillation
8	Left descending artery	3 hours	Ventricular fibrillation
9	Left descending artery	1 day	Myocardial infarction
10	Left descending artery	2 days	Myocardial infarction
11	Left descending artery	4 days	Artery occluded by thrombus, myocardial infarction
12	Left descending artery	6 days	Septal artery blocked, septal infarction, infarction of the myocardial wall
13	Left circumflex artery	Immediately	Ventricular fibrillation
14	Left circumflex artery	2 days	Myocardial infarction
15	Left circumflex artery	2 days	Myocardial infarction
16	Left circumflex artery	4 days	Myocardial infarction

In the series of dogs which were operated upon with the tube implantation, the wire was inserted at the same stage as the tube in 2 dogs (Table II) The other dogs were operated upon 2 to 7 days after the wire implantation In these dogs, as a rule, we found at the second operation definite microscopic evidence of myocardial infarction, which was in most cases substantiated by electrocardiograms and the clinical state of the animal There was bluishness over the area of distribution of the pertinent artery, and at probing there was lack of myocardial tonus The vessels of the bluish area were straightened out and flattened It was felt there was a difference in contractile strength between this area and the surrounding healthy myocardium Sometimes, also, definite bulging of the ischemic area was observed and, in a few cases, there was paradoxical systole The borderline between the pathologic and the healthy looking area usually was rather sharp

TABLE II DOGS WITH EXPERIMENTALLY INDUCED CORONARY THROMBOSIS AND MYOCARDIAL INFARCTION, SUBSEQUENT IMPLANTATION OF TUBE

EXPERIMENT NO	SITE OF MG AL WIRE IMPLANTATION	TUBE INSERTED (DAYS AFTER FIRST OPERATION)	FATE OF DOG	NOTES
17	Right coronary artery	Simultaneously	Died 2 days later	Pleural empyema tube patent
18	Right coronary artery	3	Survived	
19	Right coronary artery	3	Survived	
20	Right coronary artery	4	Survived	
21	Left descending artery	Simultaneously	Died 1 day post op	Pulmonary atelectasis tube patent
22	Left descending artery	2	Survived	
23	Left descending artery	2	Survived	
24	Left descending artery	3	Survived	
25	Left descending artery	3	Died 15 days later	Abortion, tube patent, coronary art occluded old infarction
26	Left descending artery	4	Survived	
27	Left descending artery	4	Survived	
28	Left descending artery	4	Vent fibrill immediately post op	
29	Left descending artery	7	Survived	
30	Left circumflex artery	2	Survived	
31	Left circumflex artery	2	Survived	

After implantation of the nylon tube in the myocardium, no immediate changes in the color or general appearance of the ischemic area could be seen Eleven out of 15 dogs operated upon with tube implantation survived, the time of observation being at least 4 months One dog died from ventricular fibrillation *immediately after the closure of the chest* Two dogs died from pleuro pulmonary complications, in these dogs the tubes were found to be patent Another dog died 15 days after the second operation Also, in this dog the tube was found to be patent, and the myocardium was in the healing stage of infarction

At postmortem examination of the remaining dogs, myocardial infarction was observed in all cases. In 4 dogs, surviving 4 to 15 days after the wire implantation, the wire was dissolved and a thrombus was found at the site of the implantation (Fig. 1). In some other cases there was slight erosion on the surface of the wire, and there were signs of beginning thrombus formation (fibrin deposits, etc.).

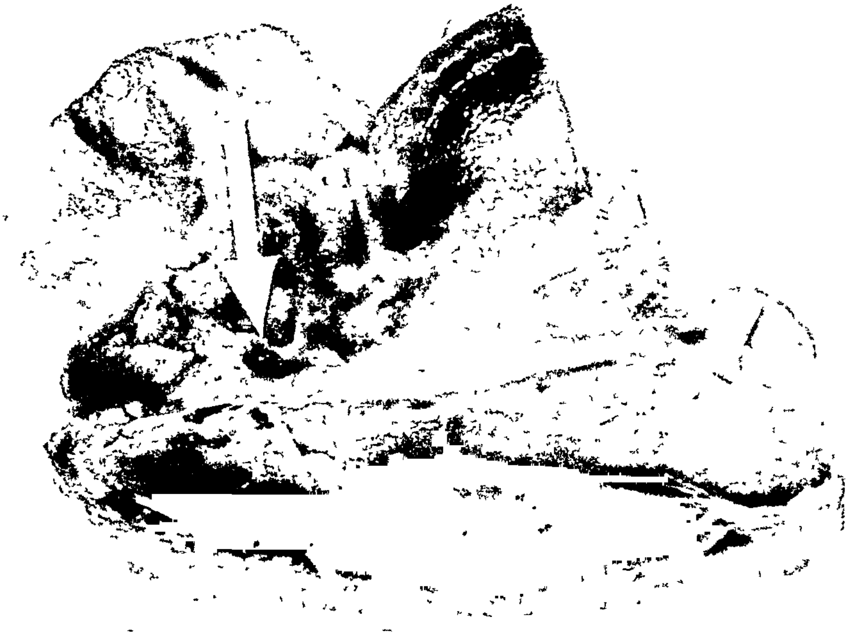


Fig. 1.—Thrombus attached to the wall (*at arrow*) of the right coronary artery 7 days after the insertion of a magnesium-aluminum alloy wire.

TABLE I. CONTROL EXPERIMENTS

EXPERIMENT NO.	SITE OF MG-AL WIRE IMPLANTATION	DEATH (TIME AFTER IMPLANTATION)	NOTES
1	Right coronary artery	1 hour	Ventricular fibrillation
2	Right coronary artery	4 hours	Severe myocardial ischemia
3	Right coronary artery	4 days	Severe myocardial infarction
4	Right coronary artery	7 days	Artery occluded by thrombus, myocardial infarction (Fig. 1)
5	Right coronary artery	8 days	Artery occluded by thrombus, myocardial infarction (Fig. 1)
6	Right coronary artery	15 days	Artery occluded by thrombus, myocardial infarction (Fig. 1)
7	Left descending artery	Immediately	Ventricular fibrillation
8	Left descending artery	3 hours	Ventricular fibrillation
9	Left descending artery	1 day	Myocardial infarction
10	Left descending artery	2 days	Myocardial infarction
11	Left descending artery	4 days	Artery occluded by thrombus, myocardial infarction
12	Left descending artery	6 days	Septal artery blocked, septal infarction, infarction of the myocardial wall
13	Left circumflex artery	Immediately	Ventricular fibrillation
14	Left circumflex artery	2 days	Myocardial infarction
15	Left circumflex artery	2 days	Myocardial infarction
16	Left circumflex artery	4 days	Myocardial infarction

In the series of dogs which were operated upon with the tube implantation, the wire was inserted at the same stage as the tube in 2 dogs (Table II). The other dogs were operated upon 2 to 7 days after the wire implantation. In these dogs, as a rule, we found at the second operation definite macroscopic evidence of myocardial infarction, which was in most cases substantiated by electrocardiograms and the clinical state of the animal. There was bluishness over the area of distribution of the pertinent artery, and at probing there was lack of myocardial tonus. The vessels of the bluish area were straightened out and flattened. It was felt there was a difference in contractile strength between this area and the surrounding healthy myocardium. Sometimes, also, definite bulging of the ischemic area was observed and, in a few cases, there was paradoxical systole. The borderline between the pathologic and the healthy looking area usually was rather sharp.

TABLE II DOGS WITH EXPERIMENTALLY INDUCED CORONARY THROMBOSIS AND MYOCARDIAL INFARCTION, SUBSEQUENT IMPLANTATION OF TUBE

EXPERIMENT NO	SITE OF MYOCARDIAL WIRE IMPLANTATION	TUBE INSERTED (DAYS AFTER FIRST OPERATION)	FATE OF DOG	NOTES
17	Right coronary artery	Simultaneously	Died 2 days later	Pleural empyema, tube patent
18	Right coronary artery	3	Survived	
19	Right coronary artery	3	Survived	
20	Right coronary artery	4	Survived	
21	Left descending artery	Simultaneously	Died 1 day post op	Pulmonary atelectasis, tube patent
22	Left descending artery	2	Survived	
23	Left descending artery	2	Survived	
24	Left descending artery	3	Survived	
25	Left descending artery	3	Died 15 days later	Abortion, tube patent, coronary art occluded old infarction
26	Left descending artery	4	Survived	
27	Left descending artery	4	Survived	
28	Left descending artery	4	Vent fibrill immediately post op	
29	Left descending artery	7	Survived	
30	Left circumflex artery	2	Survived	
31	Left circumflex artery	2	Survived	

After implantation of the nylon tube in the myocardium, no immediate changes in the color or general appearance of the ischemic area could be seen. Eleven out of 15 dogs operated upon with tube implantation survived, the time of observation being at least 4 months. One dog died from ventricular fibrillation immediately after the closure of the chest. Two dogs died from pleuropulmonary complications, in these dogs the tubes were found to be patent. Another dog died 15 days after the second operation. Also, in this dog the tube was found to be patent, and the myocardium was in the healing stage of infarction.

At postmortem examination of the remaining dogs, myocardial infarction was observed in all cases. In 4 dogs, surviving 4 to 15 days after the wire implantation, the wire was dissolved and a thrombus was found at the site of the implantation (Fig. 1). In some other cases there was slight erosion on the surface of the wire, and there were signs of beginning thrombus formation (fibrin deposits, etc.).

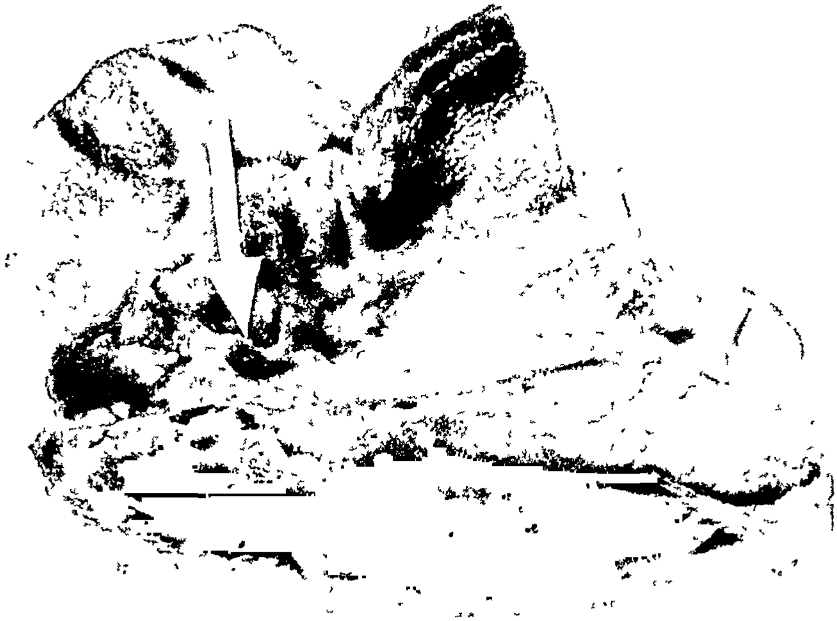


Fig 1.—Thrombus attached to the wall *(at arrow)* of the right coronary artery 7 days after the insertion of a magnesium-aluminum alloy wire.

TABLE I. CONTROL EXPERIMENTS

EXPERIMENT NO.	SITE OF Mg-Al WIRE IMPLANTATION	DEATH (TIME AFTER IMPLANTATION)	NOTES
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5	Right coronary artery	8 days	Artery occluded by thrombus, myocardial infarction (Fig. 1)
6	Right coronary artery	15 days	Artery occluded by thrombus, myocardial infarction (Fig. 1)
7	Left descending artery	Immediately	Ventricular fibrillation
8	Left descending artery	3 hours	Ventricular fibrillation
9	Left descending artery	1 day	Myocardial infarction
10	Left descending artery	2 days	Myocardial infarction
11	Left descending artery	4 days	Artery occluded by thrombus, myocardial infarction
12	Left descending artery	6 days	Septal artery blocked, septal infarction, infarction of the myocardial wall
13	Left circumflex artery	Immediately	Ventricular fibrillation
14	Left circumflex artery	2 days	Myocardial infarction
15	Left circumflex artery	2 days	Myocardial infarction
16	Left circumflex artery	4 days	Myocardial infarction

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TABLE II DOGS WITH EXPERIMENTALLY INDUCED CORONARY THROMBOSIS AND MYOCARDIAL INFARCTION, SUBSEQUENT IMPLANTATION OF TUBE

EXPERIMENT NO	SITE OF METAL WIRE IMPLANTATION	TUBE INSERTED (DAYS AFTER FIRST OPERATION)	FATE OF DOG	NOTES
17	Right coronary artery	Simultaneously	Died 2 days later	Pleural empyema tube patent
18	Right coronary artery	3	Survived	
19	Right coronary artery	3	Survived	
20	Right coronary artery	4	Survived	
21	Left descending artery	Simultaneously	Died 1 day post op	Pulmonary atelectasis tube patent
22	Left descending artery	2	Survived	
23	Left descending artery	2	Survived	
24	Left descending artery	3	Survived	
25	Left descending artery	3	Died 15 days later	Abortion tube patent, coronary art occluded, old infarction
26	Left descending artery	4	Survived	
27	Left descending artery	4	Survived	
28	Left descending artery	4	Vent fibrill immediately post op	
29	Left descending artery	7	Survived	
30	Left circumflex artery	2	Survived	
31	Left circumflex artery	2	Survived	

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A blind tube was implanted in the myocardium in 6 dogs (Table III). All of these dogs died shortly after the second operation. The longest survival was 6 days after the sham tube implantation and 10 days after the wire implantation.

TABLE III. SHAM OPERATION—BLIND NYLON TUBE IMPLANTED IN DOGS WITH SIGNS OF MYOCARDIAL INFARCTION

EXPERIMENT NO.	SITE OF Mg-Al WIRE IMPLANTATION	BLIND TUBE INSERTED (DAYS AFTER FIRST OPERATION)	FATE OF THE DOG	NOTES
32	Right coronary artery	4	Died 6 days after 2nd operation	Myocardial infarction
33	Right coronary artery	4	Died 1 day after 2nd operation	Myocardial infarction
34	Left descending artery	2	Died 3 hours after 2nd operation	Myocardial infarction
35	Left descending artery	3	Died 1 day after 2nd operation	Ventricular fibrillation
36	Left descending artery	3	Died 3 days after 2nd operation	Severe myocardial infarction
37	Left descending artery	3	Died 3 days after 2nd operation	Severe myocardial infarction

Summing up, in a control series with induced coronary artery occlusion and myocardial infarction, the mortality was 100 per cent. In a similar series, treated with intramyocardial implantation of a nylon tube carrying blood from the internal mammary artery, the rate of survival was 11 out of 15 animals (73 per cent). When a sham procedure was undertaken with a closed nylon tube in 6 animals, all died within 6 days of the sham operation.

DISCUSSION

If a magnesium-aluminum wire is inserted into a major coronary artery, one of three things may happen. The dog may die from ventricular fibrillation in connection with the operative procedure (it is well known that manipulations and even temporary occlusion of a coronary artery often result in this complication). Second, the wire itself could obstruct the lumen, causing myocardial ischemia rather quickly after the insertion. Third, a thrombus could develop around a skeleton of metal meshwork, and this thrombus could progressively obstruct the lumen. In the control series, probably all three alternatives are represented. For a comparison with the experimental series, only the dogs with a slowly developing thrombosis are of value. In the control series, 11 such dogs are included, all of which died between the second and fifteenth day of the implantation of the wire. Judging from the findings at the second operation in the experimental series we believe it possible that these dogs also would have succumbed from their infarction within the first 2 weeks. Since these animals survived we believe the second operation prevented their death by the implantation of a tube.

In the experimental series in which a blind nylon tube was implanted, all dogs died within the same time limits as did the control dogs. This must be taken as evidence that the implanted open tubes remained patent, at least for some time, and that they effectively supplied arterial blood to the ischemic parts of the heart. In another series we investigated the patency of the tubes in the living animal at a short interval after its implantation in the myocardium,[1] and found that most of the tubes were patent within the first week. Furthermore, if the patent tubes were clamped, the animal died from myocardial infarction another piece of evidence that the implanted tube was important for the arterial supply of the heart.

As far as we know this is the first time any attempt has been made to use nylon tubes as substitution for the ordinary coronary flow in cases of experimental infarction. Smith and McIntyre,[10] however, recently published some results with Ivalon grafts from the left subclavian artery to the distal part of a ligated coronary artery and they also found most of their grafts patent. The time during which tubes of artificial material remain open seems to be adequate to help the ischemic part of the myocardium over the critical period, i.e., the time required for the dog to develop functioning extra- and intracardiac anastomoses. This time has been calculated to be between 4 and 12 days.[11] Ultimately, however, the tubes get obstructed. If intramyocardial implantation of nylon tubes, or tubes of another inert material should ever be attempted in man, it, therefore, should be combined with some other method of revascularization of the myocardium. Intrapericardial poudrage, cardiopneumopexy, or possibly ligation of the contralateral internal mammary artery could be considered as relevant procedures.

The tubes were implanted in the borderline between the ischemic area and the apparently healthy myocardium. This was done for two reasons. First, it proved to be the best place for technical reasons since sutures were likely to cut through the damaged tissue of the ischemic area. Second, it probably is of importance to supply the border zone since it was shown by Harris and Rojas[12] that the ectopic foci which lead the heart into ventricular fibrillation following occlusion of a coronary artery, as a rule, are situated in this zone. Probably a slight increase of the arterial blood supply to this region will be most helpful to prevent early ventricular fibrillation.

SUMMARY

Artificial coronary thrombosis was created in dogs by the insertion of a magnesium-aluminum alloy wire in one of the major coronary arteries. In 16 dogs no further treatment was undertaken; all of these animals died within 15 days after the wire implantation. In 17 dogs electrocardiographic and/or clinical evidence of myocardial ischemia was found following the wire

implantation. These dogs were reoperated upon on the second to seventh day after the first operation. A nylon tube was inserted into the internal mammary artery and its other end buried in the border zone between the healthy and the ischemic myocardium. The dogs operated upon with this procedure survived a manifest myocardial infarction to 73 per cent (11 out of 15 animals). In 6 dogs, the same procedure was undertaken, but the implanted tube was closed. All these dogs died within 6 days after the second operation.

It is concluded that the intramyocardial implantation of a nylon tube carrying blood from the internal mammary artery, at least for some time, is effective in maintaining the necessary arterial blood supply to the ischemic area of the myocardium, and this procedure was contributory to the survival of the dog.

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THE ASSOCIATION OF HIATUS HERNIA AND GASTROESOPHAGEAL MALIGNANCY

Richard H. Adler, M.D., and Jose Rodriguez, M.D., Buffalo, N. Y.

The association of hiatus hernia and gastroesophageal malignancy has been a subject of interest in recent years. Whether this association is merely a coincidence or whether there is a cause and effect relationship remains unsettled. For example, Brick[5] stated, in 1949, that, "The chances of a patient with hiatus hernia developing a carcinoma of the stomach was four times less than in patients without a hiatus hernia." It was his impression that, "The hiatus hernia itself affords some protection against gastric cancer just as duodenal ulcer appears to protect the patient against gastric cancer." In 1952, Pack and his co-workers[11] reported 2 cases of total intrathoracic stomachs with gastric carcinoma. These authors postulated that the theoretical likelihood of a patient with a diaphragmatic hernia developing cancer within the intrathoracic stomach was about 1 in 180,000. That same year, Feldman and Myers[7] reported 3 cases of esophageal hiatus hernia with gastric carcinoma and found an additional 43 cases recorded in the literature. They concluded that the incidence of gastric carcinoma was not significantly greater in those with hiatus hernia than in those without herniation. Smithers,[16] however, in 1955, reviewed 108 recorded cases of esophageal hiatus hernia and associated gastroesophageal malignancies, including 20 cases of his own. It was his impression that the combination of hernia and tumor due to chance was unlikely That same year, Tanner[18] reported 25 cases of his own and stated that, "I have found this association so often that I wonder whether reflux esophagitis might not be a cancer provoking lesion."

From the Buffalo General Hospital and the Roswell Park Memorial Institute, and the Department of Surgery, The University of Buffalo School of Medicine, Buffalo, N. Y.

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Recent experience with several cases of hiatus hernia with gastric and esophageal malignancy stimulated our interest in this association. All available literature on the subject has been reviewed. Smithers presented a collective review of all published cases in 1955.[16] A number of other reports have appeared during the last several years.[3, 4, 6, 8-10, 12, 13, 15, 17, 18, 20] In addition, cases of hiatus hernia with gastroesophageal malignancy have been uncovered in publications not concerned specifically with this association. The number of cases included in our review is listed in Table I.

TABLE I. CASES OF HIATUS HERNIA AND SHORT ESOPHAGUS WITH ASSOCIATED GASTROESOPHAGEAL MALIGNANCY

AUTHOR	DATE	ADENO-CARCINOMA	SQUAMOUS-CELL CARCINOMA	SARCOMA	HISTOLOGY?	TOTAL
Polley	1941	2	—	—	—	2
Smithers (collected review)	1870-1955	37	9	5	57	108
Tanner	1955	16	9	—	—	25
Pattinson	1955	9	—	—	—	9
Smith	1955	1	—	—	—	1
Wiley	1956	6	1	—	4	11
Dunlop	1956	7	3	—	—	10
Kay and Cross	1956	5	2	—	—	7
Mobley & Christensen	1956	—	—	—	1	1
Blades & Hall	1956	1	—	—	—	1
Friedman	1957	2	—	—	—	2
Peters	1958	3	—	—	—	3
Sparks	1958	—	—	—	9	9
Boyd et al.	1958	—	1	—	—	1
Adler & Rodriguez	1958	15	6	1	—	22
Totals		104	31	6	71	212

Some cases were lacking in specific details, such as neoplastic cell type and exact tumor location, but, in a few instances, this information was acquired through other references. It should be emphasized that our listing does not represent the total number of cases of hiatus hernias with gastroesophageal malignancies reported in the literature. It was not practical to review every publication on subjects such as reflux esophagitis, short esophagus, and diaphragmatic hernia in an effort to uncover additional scattered cases of hiatus hernia associated with gastroesophageal malignancy that may have received only passing comment in publications not concerned with this association. Nor was it feasible to include a meaningful analysis of the foreign literature. Therefore, this paper will concentrate on the English language literature and our own data.

CLINICAL DATA

All cases of hiatus hernia, primary malignancy of the stomach, and primary malignancy of the esophagus from the Buffalo General Hospital and the Roswell Park Memorial Institute for the 11-year period January, 1947, through December, 1957, have been reviewed. The Roswell Park Memorial Institute is a state hospital for neoplastic diseases and provides excellent facilities for complete studies of gastric and esophageal malignancies. The Buffalo General Hospital has active private and ward teaching services and presents a somewhat less specialized sampling from the general population. It seemed quite natural to combine the data from these two hospitals because of their geographic proximity and the authors' associations with each institution.

During this 11-year period, there were 697 hospital admissions with gastric malignancy; 388 to the Buffalo General Hospital and 309 to the Roswell Park Memorial Institute. Seven malignancies were sarcomas and the rest were carcinomas. Special attention was directed to malignancies involving the gastric cardia since this area of the stomach is particularly disturbed in hiatus hernia. Unfortunately, an exact definition of the term cardia is lacking, due to the fact that the area is without absolute anatomic landmarks and a concept of what the word refers to differs among individuals. For purposes of this study, however, the cardia was arbitrarily chosen to mean the area of stomach extending approximately 4 to 5 cm. inferiorly from the gastroesophageal junction. Not all tumors were confined entirely to this area, and many involved varying amounts of distal stomach as well. In larger tumors, it was usually impossible to be certain whether the tumor actually arose from the cardia or involved it by extension. Unless the tumor extended to the gastroesophageal junction, however, it was not considered as a malignancy involving the cardia. For example, a tumor involving the gastric fundus but not in close proximity to the gastroesophageal junction would not be included as a tumor involving the cardia. The location of the tumor was determined on the basis of radiographic, surgical, and pathologic descriptions. Of the 697 gastric malignancies, 121 (17.3 per cent) involved the gastric cardia.

There were 302 hospital admissions for primary esophageal malignancy during this period; 97 to the Buffalo General Hospital and 205 to the Roswell Park Memorial Institute. As with the gastric malignancies, the cases in which the diagnoses were in question were not included in this analysis. For example, there were 243 cases of probable esophageal malignancy at the Roswell Park Memorial Institute during this period, but only the 205 cases verified histologically were included in this study. Three of the 302 esophageal malignancies were sarcomas; the rest were carcinomas. Twenty-one of the malignancies involved the cervical esophagus. The distal one third of the intrathoracic esophagus received special attention since this area is particularly exposed to the irritating effects of gastroesophageal reflux and obstructive stagnation that may be associated with hiatus hernia. Normally this segment would include approximately the distal 8 cm. of the intrathoracic esophagus or that part beyond the level of the inferior pulmonary vein. In practice, however, these areas could not always be rigidly defined, especially in the presence of a large hiatus hernia. A special effort was also made to classify neoplasms as to location and cell type rather than have a vague group of "cardioesophageal" tumors. This was accomplished by analyzing all available information obtained by x-ray, esophagoscopy, surgery, and autopsy. Of the 302 esophageal malignancies, 73 (24.1 per cent) involved the lower third of the intrathoracic esophagus.

A total of 814 patients with hiatus hernia were admitted to both hospitals during this period; 676 to the Buffalo General Hospital and 138 to the Roswell Park Memorial Institute. Most hernias were diagnosed by x-ray studies and some were verified at surgery. Five cases of hernia at the Buffalo General Hospital and 10 of the Roswell Park Memorial Institute group were of the parahiatal type. These were included in the review although they differ in certain respects from the sliding hiatus hernia. Unfortunately, not all roentgenograms were available for our review; in this situation the radiologist's report was used. Many of these cases have been carefully analyzed as part of another study on hiatus hernia,[19] but the entire group was not thoroughly reviewed for symptomatology. In those analyzed, however, there was little *correlation between hernia size and severity* of symptoms.

Certain interesting findings followed further analysis of the hernias. There were 505 females and 309 males. Of the total 814 hernias, 21 (2.5 per cent) had an associated gastroesophageal malignancy. Their distribution is shown in Table II. One patient (Case 10), although seen in 1957, was not included in the 11-year analysis ending December, 1957, because surgery was not performed until early 1958.

TABLE II. GASTROESOPHAGEAL MALIGNANCY WITH ASSOCIATED HIATUS HERNIA LOCATION AND HISTOLOGY (B.G.H. AND R.P.M.I.)

LOCATION	ADENO-CARCINOMA	SQUAMOUS-CELL CARCINOMA	SARCOMA	TOTAL
Esophagus (Intrathoracic)				9
Upper third	—	2	—	
Middle third	—	1	—	
Lower third	2	3	1	
Stomach				12
Cardia (primarily)	8	—	—	
Cardia (plus distal involvement)	4	—	—	
Totals	14			21

When these 21 cases of hiatus hernia associated with gastric or esophageal malignancy were examined from the aspect of sex incidence, a definite difference was noted. There were 309 males with hiatus hernia of which 16 (5.1 per cent) had an associated malignancy, whereas only 5 (0.9 per cent) of the 505 females with hiatus hernia had an associated gastroesophageal malignancy.

Because the gastric cardia and distal esophagus are sites that should be most affected by any deleterious effects associated with hiatus hernia, these areas were examined further. Of 121 malignancies involving the gastric cardia, 12 (9.9 per cent) had an associated hiatus hernia. There were 73 malignancies of the distal one third of the intrathoracic esophagus, of which 6 (8.2 per cent) had an associated hiatus hernia. This made a total of 194 cases with malignancies involving the gastric cardia and distal esophagus, of which 18 (9.2 per cent) had an associated hiatus hernia.

CASE REPORTS GASTROESOPHAGEAL MALIGNANCIES WITH ASSOCIATED HIATUS HERNIAS

I *Gastric Malignancies With Associated Hiatus Hernias*—

CASE 1—H S, a 38 year old white woman was admitted to B G H on July 20, 1948, *complaining of dysphagia for 6 months with a 20 pound weight loss, and vomiting for the previous 10 days* Esophagogram performed elsewhere 3 months prior to admission, had been interpreted as showing stenosis involving the lower esophagus When the roentgenograms were reviewed, a hiatus hernia was noted At esophagoscopy, a tumor that bled easily was encountered at a level corresponding to the area of stenosis seen on the x ray films On biopsy, this proved to be an adenocarcinoma At surgery on July 28, 1948, the *cardia was found herniated through a patulous hiatus The tumor involving the cardia* and extending to the distal esophagus was resected The surgeon felt that this probably represented a congenitally short esophagus with a gastric carcinoma

CASE 2—W F a 58 year old white man was admitted to B G H on Aug 5, 1948, with complaints of epigastric gas pains and fatty food intolerance for the past 4 months He claimed that he had had "an uneasy stomach for many years " X ray studies on Aug 8 1948, showed a hiatus hernia and tumor thought to involve the distal esophagus X ray studies elsewhere, 2 months previously, had shown a hiatus hernia At esophagoscopy, on August 10, the endoscopist felt that the cardia was above the level of the diaphragm A friable, granular mass was seen extending into the distal esophagus which on biopsy proved to be an anaplastic papillary adenocarcinoma A nonresectable tumor involving the cardia and distal esophagus was found at surgery on Aug 30, 1948 There was no mention of a hiatus hernia in the operative report

CASE 3—J G, a 47 year old white man, was admitted to B G H on Dec 28, 1948 because of dysphagia, substernal sticking of food and vomiting for the previous 3 months X ray studies at that time showed the presence of cardiospasm Nothing abnormal was found on esophagoscopy The patient was discharged and re admitted on March 7, 1949, because of progressive dysphagia and a 25 pound weight loss Esophagoscopy on March 7 revealed prominent inflammatory folds in the lower esophagus that bled easily A biopsy taken from this area showed edema and congestion Roentgenograms on March 14 were interpreted as showing a congenitally short esophagus with hiatus hernia and an obstructing lesion thought to be on an inflammatory basis Because dysphagia persisted, despite esophageal dilatation, surgery was performed on April 1, 1949 An unsuspected tumor was found at the cardioesophageal junction This was resected and found to be an adenocarcinoma arising from the cardia The operative report did not mention the hiatus hernia

CASE 4—R R, a 51 year old white man, was admitted to B G H on Jan 21, 1952, because of dysphagia, substernal pain, and regurgitation of 2 months' duration X ray studies on January 23 revealed "a hiatal hernia with a filling defect in the cardia consistent with malignancy " Esophagoscopy revealed nothing abnormal in the esophagus except for a moderate amount of "cardiospasm " At surgery, on Jan 26, 1952, a tumor was found involving the cardia and the hiatus The tumor was resected and this proved to be an adenocarcinoma The surgeon did not mention the hiatus hernia in his operative report

CASE 5—G B, a 61 year old white man, was admitted to B G H on Jan 11, 1953, complaining of solid food sticking in his throat for the previous 3 weeks X ray studies revealed a hiatus hernia and a lesion interpreted as esophageal polyp (Fig 1) At esophagoscopy, a papillary tumor was found 40 cm from the upper incisor teeth and biopsy revealed it to be an infiltrating adenocarcinoma At surgery, on Jan 15, 1953, a tumor of the cardia extending to the distal esophagus was found and resected Examination of the surgical specimen confirmed the diagnosis of adenocarcinoma The hiatus hernia was not mentioned in the operative report

CASE 6.—A. M., a 68-year-old white man, was admitted to R. P. M. I. on July 26, 1955, because of dysphagia, low substernal pains, and food sticking in the lower chest for approximately 2 months. X-ray studies on July 26 revealed a filling defect within a hiatus hernia. Esophagoscopy at that time showed edematous hyperemic gastric mucosa with superficial ulcerations, 36 cm. from the upper incisors. No tumor was seen. Esophagoscopy was repeated on Sept. 23, 1955, again revealing edematous gastric mucosa at the 35 cm. level with a distinct change from esophageal to gastric mucosa. No tumor was seen. Roentgenograms made on Dec. 20, 1955, showed a lesion within the herniated portion of the stomach extending to the lower esophagus. Esophagoscopy at this time revealed induration at the 38 cm. level without a definite tumor mass. The biopsy report was for mucous membrane. X-ray studies on Jan. 5, 1956, again showed a polypoid filling defect now involving the lower esophagus and extending to the gastric fundus. The hiatus hernia was not noted at this time. At surgery, a nonresectable tumor was found invading the cardia and extending to the esophagus. The histologic diagnosis was carcinoma of the stomach. The operative report made no note of a hiatus hernia.

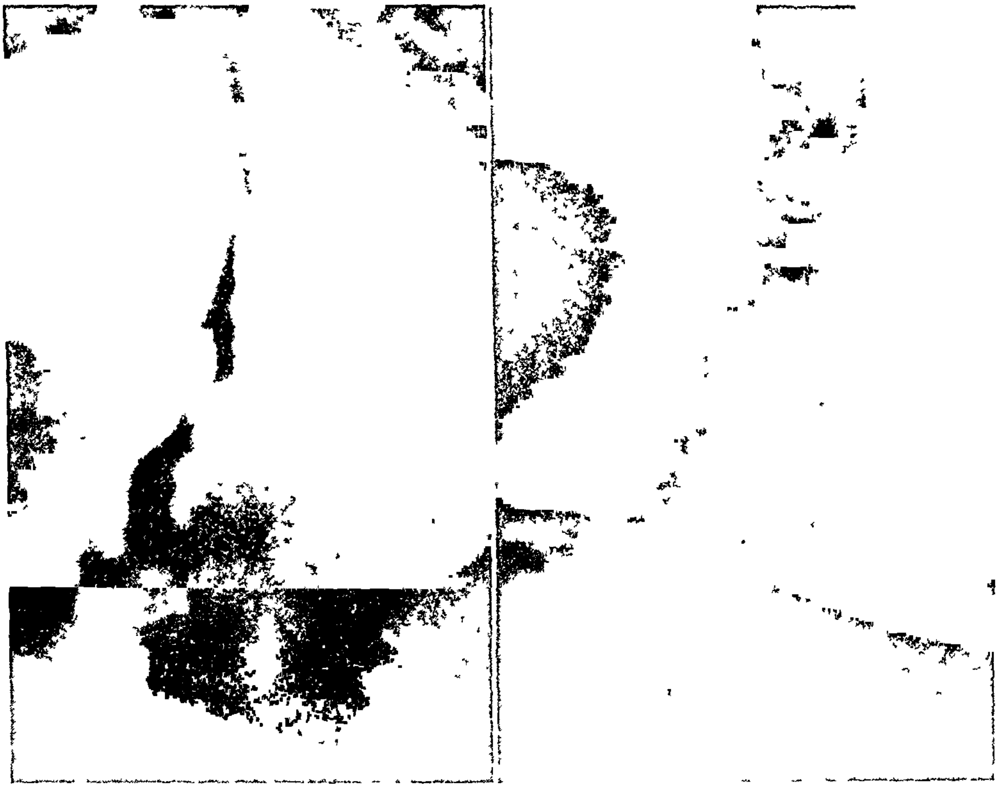

FIG. 1.—Case 5. Two x-ray views of hiatus hernia from patient with adenocarcinoma of cardia. Malignancy not suspected radiographically. Note filling defects in hernia due to tumor (see text).

CASE 7.—S. S., a 60 year-old white man, was admitted to R. P. M. I. on Oct. 8, 1954, because of abdominal gas pains radiating to the chest for the past 2 months. Roentgenograms on October 29 were described as showing that the proximal stomach herniated through the diaphragmatic hiatus with what was interpreted as a paraesophageal hernia. Unfortunately, these films were not available for us to review. The patient was subsequently admitted to another hospital in August, 1955, because of anorexia, weight loss, and emesis. Exploration revealed generalized carcinomatosis with a tumor involving the cardia and lesser curvature of the stomach. The records did not reveal whether a hiatus hernia had been noted at the time of surgery.

CASE 8.—A. D., a 66-year-old Negro woman, was admitted to R. P. M. I. on March 14, 1955, because of left upper abdominal and flank pains radiating to the left subscapular region and a 15-pound weight loss during the previous several months. A firm mass could be palpated in the upper abdomen. X ray studies revealed a hiatus hernia with multiple filling defects in the cardia and mid stomach. Esophagoscopy was not done. At surgery, a carcinoma involving the cardia and most of the stomach was found. The pathologic diagnosis was carcinoma of the stomach. The operative report made no mention of a hiatus hernia.

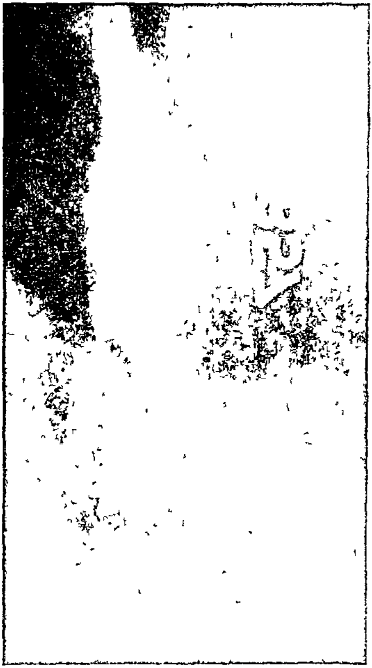

Fig 2—Case 10 Roentgenogram of hiatus hernia with gastric carcinoma involving herniated cardia Carcinoma not suspected initially, but coarse irregular mucosal folds noted by another radiologist aroused suspicion of cancer in the hiatus hernia (see text)

CASE 9.—L. M., a 66 year-old white man, was admitted to R. P. M. I. on March 9, 1956, because of epigastric distress, gas pains, and belching for the previous 3 months. On Jan. 8, 1956, he had been admitted to another hospital because of upper abdominal pains of 2 weeks' duration. Gastrointestinal x-ray studies showed a hiatus hernia and a pressure defect in the second portion of the duodenum, diagnosed as subacute pancreatitis. The patient died at R. P. M. I. without surgery, and autopsy disclosed a carcinoma involving the cardia and lesser curvature of the stomach. A cyst of the pancreas was responsible for the duodenal distortion noted in the x-ray studies. The pathologist made no mention of the hiatus hernia in his autopsy report.

CASE 10.—C. S., a 49 year old white man, was admitted to B. G. H. on Jan. 23, 1958, because of dysphagia, epigastric pain, vomiting, frequent eructations, and a 40-pound weight loss of 3 to 4 months' duration. X-ray films from another hospital taken on Oct. 1, CASE 6.—A. M., a 68-year-old white man, was admitted to R. P. M. I. on July 26, 1955, because of dysphagia, low substernal pains, and food sticking in the lower chest for approximately 2 months. X-ray studies on July 26 revealed a filling defect within a hiatus hernia. Esophagoscopy at that time showed edematous hyperemic gastric mucosa with superficial ulcerations, 36 cm. from the upper incisors. No tumor was seen. Esophagoscopy was repeated on Sept. 23, 1955, again revealing edematous gastric mucosa at the 35 cm. level with a distinct change from esophageal to gastric mucosa. No tumor was seen. Roentgenograms made on Dec. 20, 1955, showed a lesion within the herniated portion of the stomach extending to the lower esophagus. Esophagoscopy at this time revealed induration at the 38 cm. level without a definite tumor mass. The biopsy report was for mucous membrane. X-ray studies on Jan. 5, 1956, again showed a polypoid filling defect now involving the lower esophagus and extending to the gastric fundus. The hiatus hernia was not noted at this time. At surgery, a nonresectable tumor was found invading the cardia and extending to the esophagus. The histologic diagnosis was carcinoma of the stomach. The operative report made no note of a hiatus hernia.

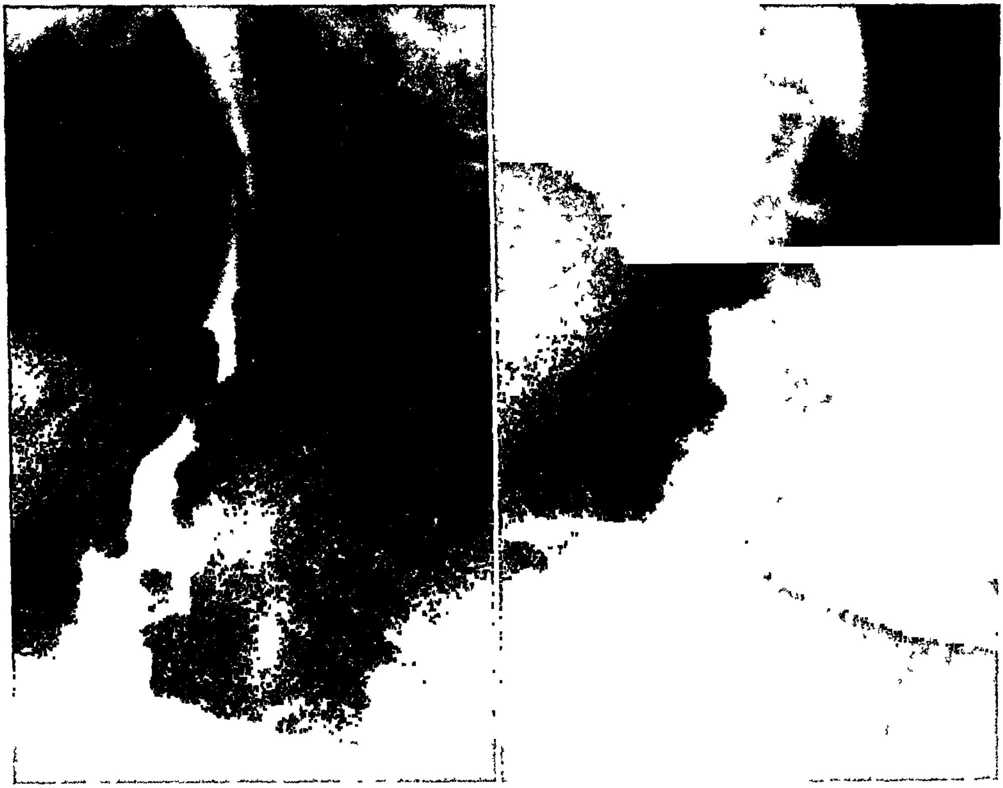

Fig. 1.—Case 5. Two x-ray views of hiatus hernia from patient with adenocarcinoma of cardia. Malignancy not suspected radiographically. Note filling defects in hernia due to tumor (see text).

CASE 7.—S. S., a 60-year-old white man, was admitted to R. P. M. I. on Oct. 8, 1954, because of abdominal gas pains radiating to the chest for the past 2 months. Roentgenograms on October 29 were described as showing that the proximal stomach herniated through the diaphragmatic hiatus with what was interpreted as a paraesophageal hernia. Unfortunately, these films were not available for us to review. The patient was subsequently admitted to another hospital in August, 1955, because of anorexia, weight loss, and emesis. Exploration revealed generalized carcinomatosis with a tumor involving the cardia and lesser curvature of the stomach. The records did not reveal whether a hiatus hernia had been noted at the time of surgery.

Case 8—A D, a 66 year old Negro woman, was admitted to R P M I on March 14, 1955, because of left upper abdominal and flank pains radiating to the left subscapular region and a 15 pound weight loss during the previous several months A firm mass could be palpated in the upper abdomen X ray studies revealed a hiatus hernia with multiple filling defects in the cardia and mid stomach Esophagoscopy was not done At surgery, a carcinoma involving the cardia and most of the stomach was found The pathologic diagnosis was carcinoma of the stomach The operative report made no mention of a hiatus hernia

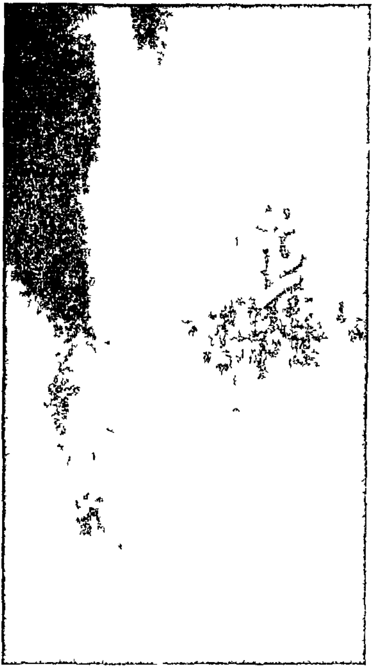

Fig 2—Case 10 Roentgenogram of hiatus hernia with gastric carcinoma involving herniated cardia Carcinoma not suspected initially but coarse irregular mucosal folds noted by another radiologist aroused suspicion of cancer in the hiatus hernia (see text)

Case 9—L M, a 66 year old white man, was admitted to R P M I on March 9, 1956, because of epigastric distress, gas pains, and belching for the previous 3 months On Jan 8, 1956, he had been admitted to another hospital because of upper abdominal pains of 2 weeks' duration Gastrointestinal x ray studies showed a hiatus hernia and a pressure defect in the second portion of the duodenum, diagnosed as subacute pancreatitis The patient died at R P M I without surgery, and autopsy disclosed a carcinoma involving the cardia and lesser curvature of the stomach A cyst of the pancreas was responsible for the duodenal distortion noted in the x ray studies The pathologist made no mention of the hiatus hernia in his autopsy report

Case 10—C S, a 49 year old white man, was admitted to B G H on Jan 23, 1958, because of dysphagia, epigastric pain, vomiting, frequent eructations, and a 40 pound weight loss of 3 to 4 months' duration X ray films from another hospital taken on Oct 1, 1957, were interpreted as showing a hiatus hernia. On admission to B. G. H., new x-ray films were obtained and the previous films reviewed. Because of the coarse, irregular mucosal folds in the hiatus hernia, the possibility of an associated carcinoma was raised (Fig. 2). Esophagoscopy on Jan. 29, 1958, revealed a papillary, easily bleeding lesion at a level 40 cm. from the upper incisors. The biopsy showed a mucous secreting carcinoma. At surgery, on Feb. 5, 1958, a tumor was found involving the cardia and proximal lesser curvature of the stomach. This filled the diaphragmatic hiatus and extended to the distal esophagus. The lesion was widely resected. Even though roentgenograms had shown a hiatus hernia to be present, this could have been easily overlooked at surgery because of the tumor.

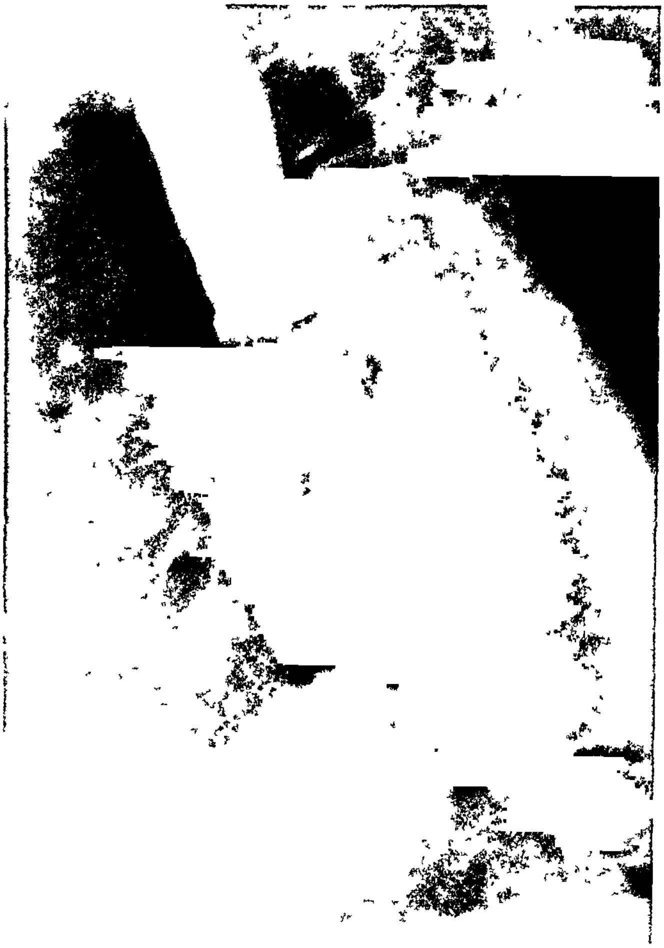

Fig. 3.—Case 11. Roentgenogram of adenocarcinoma of distal esophagus with hiatus hernia. An ulcer had been seen in the distal esophagus 19 years before at esophagoscopy (see text).

II. *Esophageal Malignancies With Associated Hiatus Hernias.*—

CASE 11.—H. D., a 70-year-old white woman, was admitted to B. G. H. on June 22, 1952, because of dysphagia, epigastric pains, and belching. She had had similar complaints intermittently for 19 years. Esophagoscopy and biopsy in 1933 showed an ulcer in the lower esophagus. Roentgenograms taken prior to admission showed an obstructing lesion in the distal esophagus with a hiatus hernia (Fig. 3). Esophagoscopy on June 24 revealed a papillary, easily bleeding tumor almost completely filling the esophageal lumen at the 25 cm. level. Biopsy showed papillary adenocarcinoma. The patient was then taken to surgery where a carcinoma involving the distal 6 cm of the esophagus was found and resected The pathologic diagnosis was mucous secreting adenocarcinoma The hiatus hernia was not mentioned in the operative report This lesion was definitely in the distal esophagus and proximal to the esophagogastric junction

CASE 12—J W, a 56 year old white man was admitted to B G H on Feb 10, 1954, because of dysphagia and a 12 pound weight loss over a period of 5 months X ray studies on February 11 showed a smooth, conical narrowing of the esophagus near the aortic arch level A hiatus hernia was noted extending 2 inches above the diaphragm Esophagoscopy on February 19 showed a concentric narrowing of the esophagus with intact mucosa This area was biopsied, however, and squamous cell carcinoma was seen on histologic examination No further operative procedures were performed This was classified as a carcinoma of the middle third of the intrathoracic esophagus

CASE 13—M S, a 77 year old white woman, was admitted to R P M I on Dec 23, 1954, because of dysphagia of 4 months' duration and a 10 pound weight loss A diagnosis of pernicious anemia had been made in 1944 X ray studies on December 31 showed a constriction of the distal esophagus and a hiatus hernia Esophagoscopy on the same day revealed a friable mass at the 26 cm level Biopsy showed normal esophageal mucosa Repeat esophagoscopy and biopsy on Jan 5, 1955 revealed epidermoid carcinoma at the same level Surgery was not done because of the patient's poor general condition

CASE 14—R P, a 59 year old white man, was admitted to B G H on Nov 2, 1955, because of heartburn, dysphagia, and substernal pain for the past month This was associated with a 15 pound weight loss Roentgenograms revealed a superior mediastinal mass posterior and to the right of the trachea Esophagogram showed a perforation in the upper intrathoracic esophagus at this area A hiatus hernia was also present Esophagoscopy disclosed a tumor with a secondary tracheoesophageal fistula which on biopsy proved to be a squamous cell carcinoma of the esophagus The abscess was drained through the neck and no further surgical procedure was performed

CASE 15—A D, a 58 year old white man, was admitted to B G H on July 9, 1956, because of progressive dysphagia for 6 months Esophagograms on July 11 showed an annular lesion in the proximal third of the intrathoracic esophagus and a small hiatus hernia Esophagoscopy revealed an esophageal tumor 20 cm from the incisors Biopsy showed this to be a squamous cell carcinoma No further surgery was performed

CASE 16—A A, a 55 year old white man, was admitted to B G H on Dec 11, 1955, because of dysphagia, excessive eructation after meals, and a 15 pound weight loss of 3 months' duration X ray studies on December 11 revealed a hiatus hernia with a short esophagus Esophagoscopy on December 13 showed a normal appearing, shortened esophagus that entered the stomach at a level interpreted to be above the diaphragm The patient was re admitted on Dec 19, 1956, because of a left lower mediastinal mass seen on x ray films He was taken to surgery on Dec 20, 1956, and a large, nonresectable tumor was encountered involving the terminal esophagus Liver metastases were present A biopsy was interpreted as leiomyosarcoma Repeat barium x rays on May 7, 1957, showed the tumor but the hiatus hernia was no longer demonstrable

III *Hiatus Hernia With, but Preceding, Gastroesophageal Malignancy*—

CASE 17—M M, a 69 year old white woman, was admitted to B G H on May 29, 1952, because of a feeling of diffuse pressure and fullness in the upper abdomen for the previous several months X ray studies on May 30 revealed a hiatus hernia She was again admitted to the hospital on Feb 25, 1957, because of severe left lower quadrant abdominal pains of 2 days' duration Radiographic studies on February 27 showed fixation of the lesser curvature of the stomach from the esophagus to the antrum The hiatus hernia previously seen was not noted at this time At surgery, on March 16, 1957, the stomach was found to be involved with tumor extending from the esophagus to the pylorus. One of the numerous peritoneal implants was biopsied and showed metastatic carcinoma. There was no mention of a hiatus hernia in the operative report.

CASE 18.—R. J., a 68-year old Negro man, was admitted to B. G. H. on April 15, 1953, because of left upper quadrant pain persisting for 3 weeks following head and left lower chest trauma. Roentgenograms on April 18 showed a hiatus hernia (Fig. 4, *A*). The patient was kept under observation and discharged improved. On Jan. 16, 1957, he was re-admitted because of persistent crampy epigastric pain that was not relived by food, milk, or antacids. He had lost 30 pounds during the preceding 3 months. A palpable mass was noted in the mid-epigastrium. X-ray studies showed fixation of the lesser curvature of the stomach with an associated ulcer. The hiatus hernia seen previously was not noted at this time (Fig. 4, *B*). At surgery, on Jan. 22, 1957, an adenocarcinoma involving the cardia and proximal two thirds of the stomach was found. It had extended to involve the distal esophagus. The surgeon did not mention a hiatus hernia in his operative report.

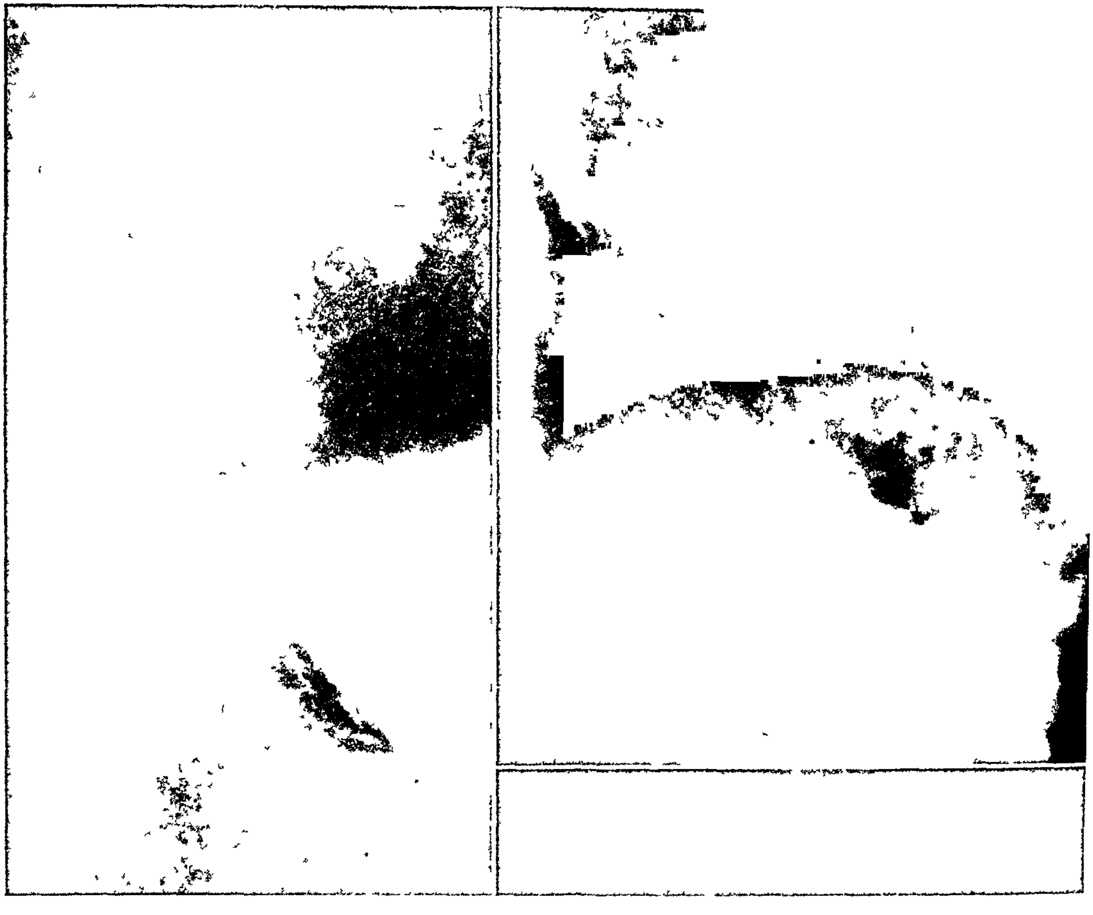
A. *B.*

Fig. 4.—Case 18 Adenocarcinoma of stomach obliterating previously demonstrable hiatus hernia. *A*, Roentgenogram (April 18, 1953) showing only hiatus hernia. *B*, Roentgenogram (Jan. 17, 1957), hiatus hernia no longer demonstrable due to tumor (see text).

CASE 19.—F. J., a 70-year-old white man, was admitted to R. P. M. I. on May 20, 1957, because of progressive dysphagia for 3 months. He was known to have had a hiatus hernia for many years. Roentgenograms before admission on May 7, 1957, revealed a hiatus hernia with a tumor thought to be in the lower esophagus. Repeat x-ray studies at R. P. M. I. showed a filling defect in the gastric cardia with a hiatus hernia. Esophagoscopy on June 14, 1957, revealed a granular, friable, ulcerating tumor. Biopsy, however, showed mucous membrane of the esophagus. At surgery, on July 15, 1957, the diaphragmatic hernia was noted to be patulous and of a size that would easily admit four fingers. The tumor was palpated in the cardia extending through the hiatus. Biopsy of a metastatic liver nodule revealed adenocarcinoma At autopsy, 6 months later, the findings of gastric carcinoma with metastases were confirmed. The hiatus hernia was not mentioned in the postmortem protocol.

CASE 20.—P. W., a 61-year old white man, was admitted to R. P. M. I. on July 7, 1947, because of occasional dysphagia, excessive gas, and a feeling of pressure in his stomach for the preceding 2 years. A lump had been present in the left side of his neck for 6 months. An x ray diagnosis of hiatus hernia had been made in 1943. X ray studies on July 9 showed a neoplasm in the lower esophagus but the hiatus hernia was not demonstrated. Esophagoscopy on July 15 showed an annular carcinoma in the distal one third of the esophagus The biopsy apparently missed the tumor and showed thickened squamous epithelium. The neck mass was then biopsied and showed metastatic carcinoma most certainly from the esophagus No further surgery was performed.

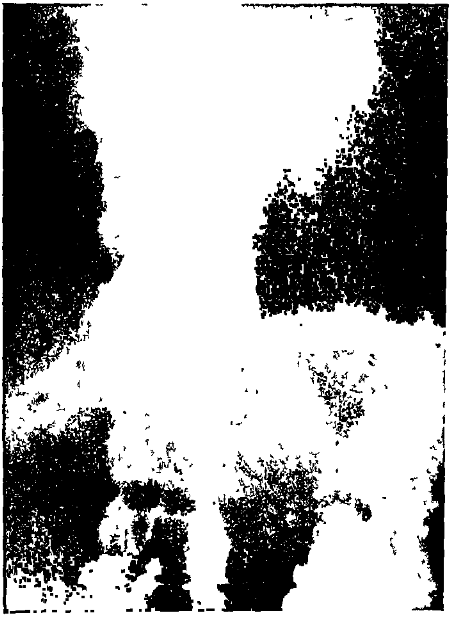

Fig 5 —Case 22 Roentgenogram of obstructing epidermoid carcinoma of distal esophagus Hiatus hernia with patulous hiatus found at surgery, although hernia not demonstrable by x-ray study (see text)

CASE 21.—F. K , a 55 year old white man, was admitted to another hospital in September, 1956, because of dysphagia, substernal pain, and vomiting for the previous month. The patient had complained of heartburn for many years, with symptoms suggesting gastro esophageal reflux. X ray studies revealed a large hiatus hernia with some narrowing and irregularity of the distal esophagus. At surgery, the hiatus hernia was noted and a tumor was palpated in the distal esophagus proximal to the gastroesophageal junction. The tumor was resected and found to be an adenocarcinoma. He was then referred to

R. P. M. I. for further management. X-ray proof of the earlier existence of a hiatus hernia is lacking, but the long history typical of gastroesophageal reflux suggests that a hernia with reflux had been present.

CASE 22.—P. D., a 67-year-old white man, was admitted to R. P. M. I. on Oct. 14, 1957, because of pyrosis, heartburn, intermittent dysphagia, substernal pain, and occasional regurgitation for 35 years. Four days prior to admission he had been unable to swallow anything. X-ray studies in 1950 were interpreted as showing esophagitis and esophageal ulcer. These impressions were confirmed by esophagoscopy and biopsy at that time. There was no note of hiatus hernia and the roentgenograms were not available for our review. X-ray studies on Oct. 23, 1957, revealed an obstructing lesion in the distal esophagus (Fig. 5). No hiatus hernia or gastroesophageal reflux was noted. Esophagoscopy revealed an ulcerating tumor, 38 cm. from the upper incisors, which was biopsied and shown to be a squamous-cell carcinoma. At surgery, a hiatus hernia was found with a patulous diaphragmatic hiatus that easily admitted three fingers. A 5 cm. tumor was found in the distal esophagus and resected. The pathologic diagnosis was squamous-cell carcinoma. Although earlier roentgenograms were lacking, the hiatus hernia with reflux esophagitis had probably been present for many years.

COMMENTS

Two other cases of hiatus hernia associated with gastric carcinoma were found in reviewing our records. They were not included here because of questionable histologic verification of the malignancy. Another patient with a symptomatic hiatus hernia of 2 years' duration was found to have an associated intramural fibromyoma of the distal esophagus which was removed at the time of hernia repair. One other patient had progressive intermittent dysphagia and had a papilloma of the distal esophagus which was proximal to a hiatus hernia and stricture. This was resected at thoracotomy and no evidence of malignancy was found.

Of the 22 cases outlined above, one (Case 10) has not been included with the 11-year statistical review because the patient was admitted to the hospital and taken to surgery 2 months after the end of the review period, although he had been seen earlier. All 12 gastric carcinomas with associated hiatus hernias involved the cardia and over one half of them were limited to the proximal stomach or cardia. Two patients showed evidence of edema and congestion at esophagoscopy verified by biopsy, one in the cardia and the other presumably in the esophagus (Cases 3, 6).

Of the nine esophageal malignancies associated with hernias, one was a leiomyosarcoma and eight were carcinomas. Two were adenocarcinomas of the distal esophagus (Cases 11, 21). Unfortunately, there was no way of checking back to see if these represented examples of carcinoma developing in the lower esophagus lined by columnar epithelium. At least 3 patients had histories of chronic illness suggesting hernias and gastroesophageal reflux (Cases 11, 21, 22). Four were definitely shown to have had hiatus hernias prior to the malignancy (Cases 17, 18, 19, 20). In only 3 patients (Cases 1, 19, 22) was a patulous hiatus or hiatus hernia noted by the surgeon. In Case 1, the surgeon thought this represented a congenitally short esophagus. The other 2 patients (Cases 19, 22) were noted by us at surgery in 1957 when our attention had become focused on the association of tumor and hernia and we specially looked for the hernia The few autopsy reports made no mention of a hernia associated with the malignancy

DISCUSSION

The association of hiatus hernia and gastroesophageal malignancy may be more common than has been thought Certain reasons as to why this association appears to be uncommon become apparent after reviewing our material Hiatus hernia itself can be considered a modern disease because it has only recently received much attention Before the use of methods for increasing the intra abdominal pressure and placing the patient in various positions many hiatus hernias were missed with upright barium examinations of the esophagus and stomach Even with present day techniques, hiatus hernia may not be seen unless the radiologist takes time and is especially interested in the subject, or unless he has been alerted to the possible presence of a hiatus hernia by the referring physician Despite special efforts by the radiologist, a hiatus hernia may not always be demonstrable at a single examination If extra time and effort are used, however, a considerable number of hiatus hernias may be found in the radiologist's practice, especially in older individuals The absence of radiologic landmarks to show the exact site of the squamous columnar mucosal junction and the hiatus margins and the functional variations in size and shape of the distal esophagus are but a few of the factors that make absolute radiologic interpretations in the gastroesophageal area and the diagnosis of hiatus hernia difficult

The presence of an obstructing neoplasm in the esophagus may divert the radiologist's attention away from further attempts to demonstrate a hiatus hernia (see Fig 5) Also, if the lesion obstructs the esophageal lumen so as to prevent sufficient passage of barium distally it may not be possible to demonstrate adequately a hiatus hernia When the tumor involves the cardia, a hiatus hernia may no longer be apparent (see Fig 4) In 4 cases from our series a hiatus hernia had been previously shown to have been present, but it was no longer demonstrable radiographically because of the intraluminal space occupying effect of the new neoplasm

Surgeons, too, may have their attention diverted away from a hiatus hernia by the presence of a tumor involving the cardia and distal esophagus This was very apparent in our cases of tumor with hernia, for the hiatus hernia was noted at surgery only when its presence became a matter for special attention With larger tumors involving the cardioesophageal area however, it may be impossible to recognize a hiatus hernia at surgery although it may have been demonstrated radiographically at an earlier date

The pathologist is seldom in a position to appreciate an antemortem hiatus herniation that has become reduced below the diaphragm at postmortem examination In addition, the steps usually followed in routine autopsy organ removal practically ruin any opportunity for detecting a sliding hiatus hernia unless the pathologist first deliberately exposes and dissects this area *In the* past, when the cardia became fixed above the diaphragm as a result of secondary fibrous esophageal shortening or adhesions, the condition was usually considered that of a congenitally short esophagus. It becomes evident, therefore, that hiatus hernias associated with gastroesophageal malignancies may have been overlooked by radiologists, surgeons, and pathologists.

In considering the association of hernia and tumor, several interesting observations come to mind. Certainly hiatus hernia is more common than previously suspected, especially when one looks for it. This is particularly true in the older age group, the age when cancer is also more common. Nevertheless, only a small number of known hiatus hernias appear to have associated gastroesophageal malignancies (2.5 per cent of our patients, 21 of 814 cases of hernia). It must be remembered, however, that many hiatus hernias are asymptomatic and may be only incidental findings in upper gastrointestinal x-ray studies. Other hernias producing symptoms are readily controlled by medical or surgical treatment. This leaves only a small number of hernias that produce continued irritations to the cardioesophageal area. Perhaps it is mainly this small number of individuals exposed to the continuous effects of irritation who may eventually develop a neoplasm. Several patients from our group of malignancies with hernias had histories of chronic heartburn, eructation, pyrosis, and dysphagia; common symptoms of gastroesophageal reflux associated with hiatus hernia. The records of others lacked this significant information, but it may have been present had it been looked for at the time.

At this time one might ask, how may a hiatus hernia predispose to gastroesophageal malignancy. An absolute answer cannot be supplied, but several considerations deserve comment. The esophagus, especially its distal part, is directly exposed to the irritating effects of refluxing gastric secretions due to gastroesophageal incompetence not uncommonly associated with hiatus hernia. It is well known that the resulting esophagitis and ulcerations may continue with repeated remissions and exacerbations. Bleeding and scarring are well-recognized complications of reflux esophagitis but not malignancy. Stasis and stagnation in the distal esophagus may also be associated with hiatus hernia as a result of spasm, edema, and stricture. A type of esophagitis may occur in the esophagus proximal to the stenosis with areas of mucosal destruction, epithelial hyperplasia, and leukoplakia. Lesions such as leukoplakia and epitheliomas may have a malignant potential but, curiously enough, interest in these intriguing relationships in the esophagus has waned during the past two decades despite the increased use of esophagoscopy and thoracic surgical procedures. The products of stagnant foods that decompose above an esophageal stricture associated with hiatus hernia may act as irritants and possibly as carcinogens. In our group of 73 patients with malignancy of the distal one third of the intrathoracic esophagus, 6 (8.2 per cent) had an associated hiatus hernia. An increased incidence of esophageal malignancy, compared to that of the general population, has also been noted with other chronic stenotic esophageal lesions, such as achalasia (cardiospasm) and lye strictures. This is an area that deserves further study.

A satisfactory explanation for a cause and effect relationship between hiatus hernia and gastric malignancy is lacking Because the proximal stomach or cardia is primarily involved as the stomach slides up through the hiatus, it might be supposed that malignant changes would be more common here Of our 12 cases of gastric carcinoma with associated hiatus hernia, eight tumors involved the cardia primarily (Table II) This is of interest but the numbers are probably too small to carry statistical significance It might be speculated, however, that the diaphragmatic hiatus may exert a constricting effect on the herniated stomach that would be further exaggerated by gaseous distention of the cardia and stomach above the hiatus Whether this could cause congestion or predispose to inflammation or ulceration remains conjectural In one patient with adenocarcinoma of the cardia and hiatus hernia (Case 6), edema, congestion, and ulcerations were seen in the cardia at esophagoscopy Gastric ulcers are known to occur in the herniated stomach but this raises the often disputed question as to whether a gastric ulcer may be a premalignant condition

Of the gastroesophageal malignancies with associated hiatus hernias, adenocarcinoma predominates over squamous or epidermoid carcinomas (Tables I, II) On the basis of past concepts that most adenocarcinomas arise from the stomach rather than the esophagus, it could be assumed that the stomach must have been the site of origin for most of these malignancies On gross inspection it is often difficult to determine for certain the origin of malignancies involving the cardioesophageal junction although, in general, a gastric carcinoma more commonly extends into the esophagus than does an esophageal carcinoma extend a significant distance distally into the stomach Nevertheless, adenocarcinomas have been known to occur in the esophagus, but these have been thought to originate from esophageal glands or islands of ectopic heterotopic gastric and columnar mucosa More recently, however, attention has been directed to the subject of persisting columnar mucosa within the esophagus that may extend upward for variable distances in continuity from the junction of gullet and stomach[1, 2, 16] The persistent embryonic type of columnar esophageal mucosa may be more common than had been previously suspected, and it may respond differently to the irritating factors associated with gastroesophageal reflux and stasis A tumor arising from this type of mucosa would probably be an adenocarcinoma rather than the traditional epidermoid tumor of squamous mucosal origin An acid pepsin ulcer in this columnar epithelium would apparently behave more like a peptic ulcer in the gastric mucosa rather than the multiple shallow, oozing ulcers *encountered in reflux esophagitis of the squamous mucosa* As in the stomach, however, only a small number of columnar mucosal ulcers should have any malignant potential

A final passing thought in considering adenocarcinomas having origin in the esophagus is the suggestion that reflux esophagitis and ulceration involving squamous mucosa may heal by a gastric or columnar type epithelium in the presence of an acid medium, as suggested by Allison and Johnstone[1] In our present state of knowledge, however, this would seem to be of little practical consideration for, as Peters[13] has pointed out, there is good histologic evidence that squamous regeneration occurs from residual islets in the distal esophagus.

Another idea to explain the association of hiatus hernia with gastroesophageal malignancy is that the malignancy is responsible for the hernia.[8, 16] This concept is based on the theory that a hiatus hernia may be caused by muscular shortening of the esophagus in response to certain stimuli apparently mediated through the vagus nerves. It has been suggested that perhaps the gastroesophageal malignancy serves as an irritating focus, stimulating the esophagus to shorten, and, in this way, the cardia is pulled up through the hiatus to produce the hernia. The tumor itself may enlarge the hiatus and predispose to hiatal herniation. Although these possibilities merit consideration, they certainly would not be the explanation in situations where the hiatus hernia had been shown to exist prior to the occurrence of the malignancy (Cases 17, 18, 19, 20).

One other aspect of interest noted in our series of gastroesophageal malignancies with hiatus hernias was the predominance of males. Of the 309 males with hiatus hernias, 16 (5.14 per cent) had gastroesophageal malignancies whereas only 5 (0.99 per cent) of the 505 females with hiatus hernias had malignancies. The significance of this is uncertain since carcinoma of the stomach and esophagus predominate in the male and hiatus hernia is apparently more common in the female.

In essence, then, we cannot supply a dogmatic answer to the question as to whether the association of gastroesophageal malignancy and hiatus hernia is one of coincidence or one of a cause and effect relationship. Some reasons as to why hiatus hernias were not diagnosed in the past and why they may have been missed more recently are mentioned. Certain interesting relationships exist between hiatus hernia and gastroesophageal malignancy that should stimulate further interest in the association of these relatively common conditions. Perhaps, with further attention directed to the subject, more exact information as to the incidence of this association and its true significance may be obtained that cannot be gathered from a review of cases in retrospect.

SUMMARY

Although absolute conclusions cannot be reached as to whether the association of hiatus hernia and gastroesophageal malignancy is one of chance or one of a cause and effect relationship, it would appear that this association may be more common than has been previously suspected. Special attention is directed to malignancies of the distal esophagus and gastric cardia and their relationship to hiatus hernia. Various factors that may have a bearing on this association are discussed. Included in the analysis is an 11-year review of all hiatus hernias and primary malignancies of the stomach and esophagus from two institutions.

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Note.—For brevity, only publications referred to in this paper have been listed. A comprehensive listing, prior to 1955, may be found in Smither's report.[16]

MIXED PARAGANGLIONIC AND FIBROMYXOMATOUS TUMORS IN THE THORACIC CAVITY

Report of a Case With Bilateral Occurrence of the Tumor at Five Years' Interval

Olavi Peräsalo, Kai Dammert, and Kari Sirola, Helsinki, Finland

In the literature, there is a small group of mediastinal tumors which are considered to originate in epithelial-like cells, or groups of cells differentiating in association with the ganglia of the vegetative nervous system. Miller[16] described, in 1924, the first neoplasm of this kind, using the term paraganglioma, since this tissue was called, at the time, paraganglionic tissue. It was originally the opinion of Kohn[10, 11] that it forms a uniform system of special structures ("ganglienartige Körperchen") in connection with the sympathetic chain and is characterized by the chromaffin reaction and the secretion of epinephrine. The principal representative of this system was the medulla of the adrenal gland, and the carotid body, or glomus caroticum, was another important factor. Since 1950, 5 other cases have been reported in which the tumor was considered to arise from the so-called aortic body and histologically to resemble the carotid body. Since inclusion of the latter in the paraganglionic system is increasingly questionable, authors have sought to avoid using the term paraganglioma. Thus, the 2 cases published by Lattes[13] were reported as nonchromaffin paragangliomas, and other writers have used the term chemodectoma.[5, 15] A few tumors of the aortic body had been previously described in dogs.[1, 17] In one of Lattes's cases, an aortic body tumor was coexistent with a tumor arising from both the carotid body and the ganglion nodosum of the vagus nerve. This was evidence substantiating the opinion already existing concerning the multiplicity of carotid body-like tumors.[12] Typical of these earlier described mediastinal tumors was also a slow, symptom-free growth, owing to which they usually were an incidental finding. We are able to describe below a new example of these tumors. This case, which at first was considered to be a case of malignant hemangioma,[18] brings to light not only their slow, expansive growth and the tendency to the occurrence of other similar independent tumors (in the manner of carotid body-like tumors), but

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From the Clinic for Thoracic Surgery, Central Hospital of the University of Helsinki (Chief: Professor O. Peräsalo).

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also their ability to attain a great size owing to the associated fibromyxomatous component, to produce clinical symptoms, and to exhibit features characteristic of local malignancy. Certain features in the histology and habits of these tumors, furthermore, seem to suggest that the relationship between these carotid body-like tumors and the paraganglionic tumors in the stricter sense is a very close one.

CASE REPORT

The patient was a woman, single, born in 1902. Her father had died of cancer of the lung. At the age of 28, she had contracted pulmonary tuberculosis. At this time, a cavity was seen in the right upper lobe and pneumothorax was maintained on the right side for 5 years. X-ray examinations in 1948, when she was 46, showed that the process was quiescent. In early 1951, the uterus and adnexa were removed because of myomas. Since she had cough and fever at this time, an x-ray examination was made and a tumor was seen in the left lung. The patient, who then was 49 years of age, was now admitted to the Clinic for Thoracic Surgery.

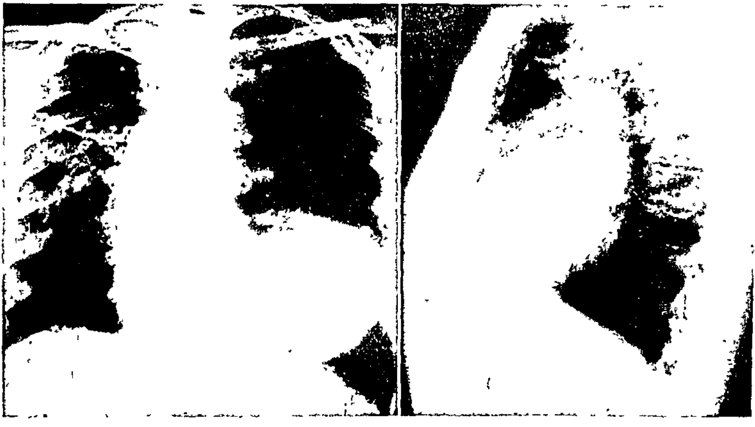

Fig. 1.—Roentgenogram, 1951. The tumor is visualized in the left lower part of the thoracic cavity.

Physical examination showed a good general condition, a plum sized nodule in the right lobe of the thyroid gland, and a blood pressure reading of 180/110 mm. Hg. The sedimentation rate was 68 mm. per hour. Roentgenologically, there were signs of old tuberculosis in the right lung and, in the lower left hemithorax, a fist-sized shadow with distinct margins, partly adjoining the heart shadow and evidently in connection with the thoracic wall (Fig. 1).

On April 4, 1951, left thoracotomy was performed (Perásalo). Situated between the lobes and adherent to them there was a fist-sized, dark, sharply circumscribed tumor, which was adherent to the anterior mediastinum and supplied by moderately large blood vessels. Extirpation of the tumor was quite readily made. Recovery was uneventful. The pathoanatomic diagnosis made at the time was malignant hemangioma.

Pathology of the Tumor Removed in 1951.—

Macroscopic: The fist-sized, dark, roundish tumor, from which a mucoid fluid exuded when cut, was enclosed in a connective tissue capsule.

Microscopic (Dammert): The tumor tissue was composed of two different components, which were separated everywhere by septa of fibrous connective tissue. One of the components was formed by epitheloid cells which, by means of delicate, highly vascular connective tissue network, formed round nests or strands (Figs. 2, *a* and *b*). The other component was loose, well-differentiated connective tissue with fusiform and stellate cells and a matrix with fine fibers (Fig. 2, *c*). The intervening septa appeared to be in firm contact with the epitheloid portion of the tumor mass (Fig. 2, *d*). Rather large, thick-walled blood vessels and small strands of epitheloid celled tumor tissue was sometimes present in the septa (Fig. 2, *a*). The cells in the nests and cords in the actual epitheloid portion were slightly variable in size. They were round or polyhedral, and occasionally cylindrical, and were closely associated with the thin-walled blood vessels of the stroma. The cell nuclei were rather large and vesicular and had a well-developed nucleolus. The cytoplasm of the cells was finely granular and frequently large and pale with indefinite margins (Fig. 2, *e*). The granules and cytoplasm did not show the specific staining by Gomori's method[7] or by the periodic acid-Schiff (PAS) method after acetylation which is specific for the chromaffin cells. Occasionally the cell nuclei were lobular or divided into two or three parts. Here and there in this organoid tissue were small accumulations of cells which resembled lymphocytes and were presumed to be sympathicogonias (Fig. 2, *f*). A few epitheloid cells in different slices were undergoing mitotic division.

The portion of the tumor consisting of fibrous connective tissue was also richly vascularized. The fibroblastic cells were mostly accumulated around the capillaries or into groups, in association with which there stood out in the intercellular tissue a larger number of collagen fibrils and more of weakly PAS-positive ground substance than elsewhere (Fig. 2, *e*).

Later Admissions.—

After the operation, the patient was in good health until, in 1956, there was an onset of lassitude and feeling of pressure in the neck and shoulder on the right. Dyspnea and palpitation occurred on exertion, with exacerbation of the symptoms she was admitted in May, 1956, to the Clinic for Thoracic Surgery. On admission, the blood pressure was 200/100 mm. Hg. The only roentgenologic finding was elevation and restricted motion of the right half of the diaphragm. Since the symptoms seemed to point to hyperfunction of the thyroid gland, an operation was performed. An "adenoma" only was found in the thyroid and was removed. The dyspnea became progressively severe, and the patient lost weight and complained of occasional pain in the right costal margin. Roentgenologic reports continued to point out relaxation of the right hemidiaphragm (Fig. 3). During hospitalization for observation, the possibility was suggested of a tumor on the right side, most likely below the diaphragm. Bronchoscopy disclosed flattening of the right lower bronchus.

She was again admitted to the Clinic in September, 1956. The blood pressure now was 170/90 mm. Hg. There was an area of absolute flatness on percussion over the anterior right hemithorax extending from the liver to the level of the third rib. The liver

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Fig. 2.—The tumor excised 1951.

a, The epitheloid part of the tumor. Note the typical organoid arrangement of the pale epitheloid cells and the slender, richly vascularized stroma. The joining fibrous connective tissue is a strong septum separating the epitheloid and the fibromyxomatous part of the tumor. In the neighborhood of the big blood vessels, note strands of epitheloid type of tumor tissue (van Gieson, ×340.)

b, The arrangement of stroma in relation to nests and cords of epitheloid cells. (Wilder stain, ×340.)

c, The fibromyxomatous part of the tumor tissue. The cells are collected around capillary vessels. The development of fine collagenic fibrils in the abundant intercellular substance. (van Gieson, ×340.)

d, Relation between the epitheloid part and the fibromyxomatous type of growth. Note the close association of the epitheloid tissue to the fibrous connective tissue septum. (van Gieson, ×41.)

e, Cellular details in the epitheloid tissue. The elongated or polyhedral cells show one to three nuclei with distinct nucleoli and a granular cytoplasm. The intimate connection between the cells and vascular stroma is well demonstrated. (van Gieson, ×1,268.)

f, Collections of sympathicogonia-like cells in the epitheloid tissue. (van Gieson, ×1,268.)

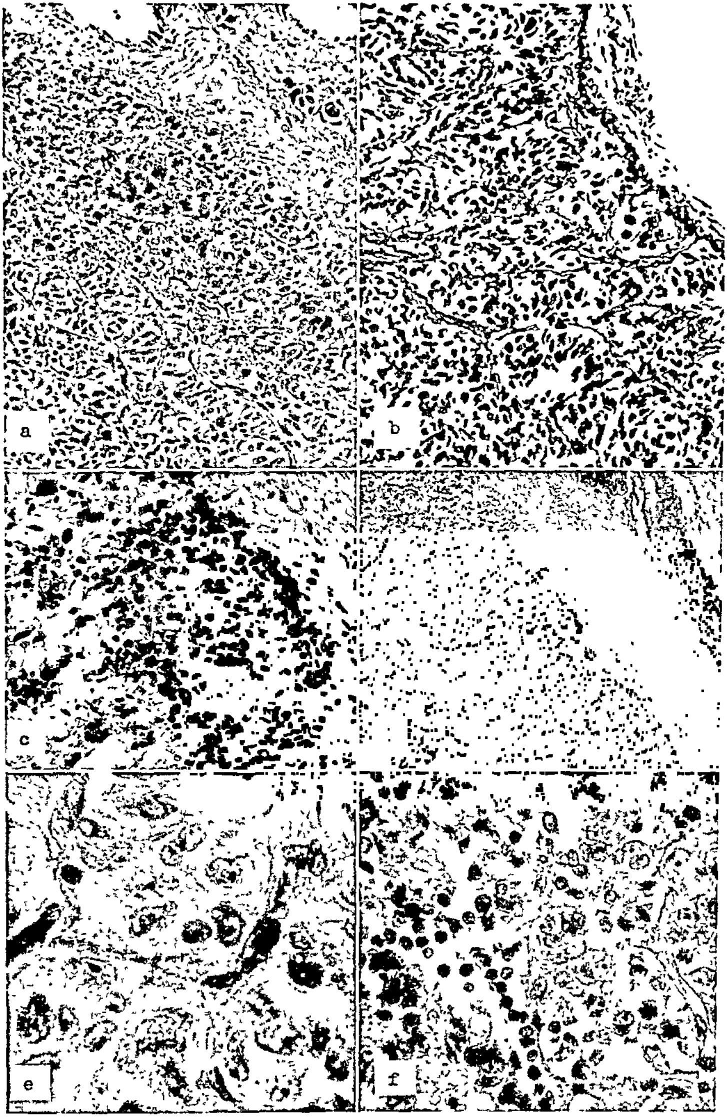

Fig 2, *a* through *f*—*For legends see opposite page.*

could be palpated anteriorly, two fingerbreadths below the costal margin. The breath sound was absent on the right, in the area of flatness. Erythrocyte sedimentation rate (ESR) was 55 mm. per hour. A right thoracotomy was performed (Peräsalo) on Sept. 12, 1956, 5½ years after the previous intrathoracic operation. A capsulated, soft, highly vascular tumor, the size of a child's head, was found to be firmly adherent to the diaphragm, which was perforated by the removal of the tumor. Postoperative recovery was uneventful and she was transferred to radiotherapy.

She has now been under the regular observation of the Radiation Clinic for 21 months, her health has been fairly good and she has been working as bookkeeper for the greater part of this time. The ESR has persisted at a rather high level (40 to 60 mm. per hour). The roentgenologic condition of the lungs is unchanged; the right half of the diaphragm has been flaccid since the operation, the lower field of the right lung shows fibrosis due to the postoperative irradiation therapy and, at the hilum of the left lung, there is the shadow of a suspected metastasis 2 by 3 cm. in size, which has not increased during the 1½ years after radiotherapy. In December, 1957, a corrosion of the seventh thoracic vertebra was found. No further changes in the bone have been observed after radiotherapy given because of a suspected metastasis here also. In May, 1958, a subcutaneous plaque, 8 cm. in diameter, was found in the interscapular region on the right and was treated by radiotherapy. However, it has not been definitely established that these findings are metastases.

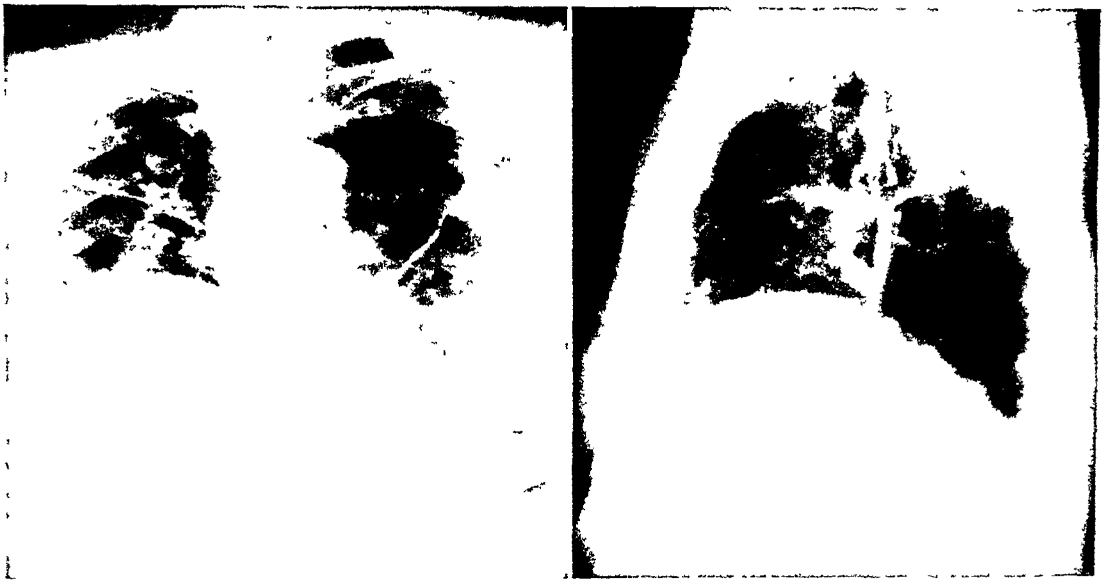

Fig. 3.—Roentgenograms, 1956. Five years after removal of the tumor on the left a new tumor is seen in the lower part of the contralateral side of the thoracic cavity.

Pathology of the Tumor Removed in 1956.—

Macroscopic: The extirpated tumor was about 15 cm. in diameter and enclosed in a strong, shiny capsule. The cut surface was rather soft, whitish or yellowish gray, with faintly discernible strands and was occasionally myxomatous. In the center of the tumor were brownish yellow, hemorrhagic or necrotic areas. The immediate subcapsular tissue was wrinkled in a manner simulating the surface of the brain.

Microscopic (Dammert): The typical components of the first growth were found also in this tumor, but they were not as distinctly differentiated. The greater part of the tumor now consisted of the fibromyxomatous component and, also, in the epitheloid portion, the stromal tissue was increased, more abundantly collagenized, and often hyalinized.

The epitheloid tissue seemed to press itself between the lobules of the fibromyxomatous portion of the tumor. The margin between the two tissue types was distinct in the superficial zones of the tumor (Fig. 4, *a*). In the regressively changed inner portions of the tumor, the collagenized and hyalinized connective tissue was greatly increased, making the differentiation of the two tissue types difficult in places. In general, the epitheloid tissue was softer and had smaller cells than that in the first tumor, and its organoid arrangement was not as evident (Fig. 4, *b*). The cells had lost much of their typical appearance. They were variable in size and shape, they had but little cytoplasm and it was poorly differentiated, and their chromatin-rich nucleus was definitely greater in relation to the size of the cell than in the earlier tumor. The cytoplasm was still finely granular and the epitheloid cells were organized similarly in relation to the vascular stroma as in the tumor removed in 1951. Mitotic figures, however, were scarcely more numerous than in the earlier tumor. The tumor tissue was attached without any distinct margin to the diaphragmatic tissue, in which nests of neoplastic cells were visible among the muscle fiber bundles. In the large fibromyxomatous lobules, the cells were small and spindle shaped and tended to become organized into groups or zones, accompanied by a stronger development of collagenic fibrils than in the corresponding tissue of the tumor excised in 1951. These formations occasionally simulated schwannomatous tissue.

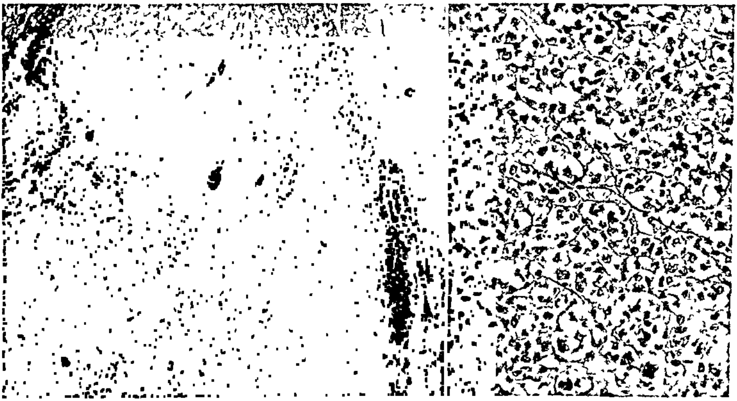

Fig. 4.—The tumor excised 1956.

a, Superficial part of the tumor showing the relation of the two tissue components participating in the tumor formation The darker parts are epitheloid, the lighter fibromyxomatous. The tissue is externally covered by a fibrous capsule. (Mallory trichrome stain, ×60.)

b, The epitheloid tissue. The organoid arrangement is present but the cells are smaller and atypic. (van Gieson, ×340)

DISCUSSION

There is no doubt but that the tumor excised in 1956 was merely a histologic variant of the one removed in 1951.* The typical organization of epitheloid structures and the absence of the staining habit of chromaffin cells justify their inclusion in the group of carotid body-like tumors, the classification of which is still largely a matter of controversy. No standard nomenclature has been accepted for these tumors. The subject has been very fully dealt with in the series Atlas of Tumor Pathology by Stout,[22] LeCompte,[14] and in the paper by Lattes.[13] Most authors appear to be of the opinion that tumors arising from chromaffin, hormonally active tissue should be termed pheochromocytomas, but no unanimity exists concerning those tumors which hormonally are inactive and which are considered to originate in nonchromaffin cells. Some authors[1, 5, 15, 17, 25] use the term chemodectoma, since they consider the deciding factor to be the function of the tissue of origin, concerning which there is some experimental evidence.[1, 20] Other investigators designate the tumors merely according to the structure of origin.[14] Lattes used the term nonchromaffin paraganglioma for tumors of the carotid body and aortic body because the cells supposed to be the origin of these tumors developed in connection with the ganglia of cranial nerves or they had an equal relationship to the parasympathetic nervous system as their relatives had to be sympathetic system; the adjective "nonchromaffin" stressed the different stainability, which could be evidence of different histogenesis and function of the former as compared with the latter. Stout[22] has been accustomed to consider the similarities in morphology and embryogenesis as a basic fact of unity of the whole tissue of this type, and the diversity of containing chromaffin granules or not as only a secondary property. According to this, he suggested the use of the term pheochromocytoma in case of hormonally active tumor, and paraganglioma in case of those hormonally inactive. Thus, his opinion concerning paragangliomas was very similar to that originally expressed by Kohn.[10, 11]

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*The authors wish to express their gratitude to the staff members of the Department of Pathology, Armed Forces Institute of Pathology, Washington, D C., for the study made in the diagnosis.

It has been difficult to determine, in the present case, the relationship between the tumors and the thoracic nervous elements but, in view of its location, the tumor excised in 1951 could well have originated in the aortic body. The tumor removed in 1956, on the other hand, could just as well have arisen from the "paraganglionic" structure of the sympathetic as of the parasympathetic nervous system. The classification of at least the latter tumor according to the tissue of origin would therefore be difficult. Considering the preceding discussion, also the names "nonchromaffin paraganglioma" and "chemodectoma" would be warranted for the tumors described. However, the observation of very immature sympathetic ganglionic cells, particularly in the tumor excised in 1951, to which these names especially well could be applied, makes one doubt the correctness of being categoric by separating them seriously from the conventional chromaffin paraganglionic group of tumors. It seems that the finding of sympathogonias was evident also in the case of Miller.[16] It is, in this connection, interesting to recall that, in the case of pheochromocytomas, different developmental stages of tumor cells are known, at least in the cases of Wahl[23] and Wahl and Robinson.[24] However, the literature seems to contain further points against the separation. These are borne out by the facts that the paragangliomas, in the stricter sense of the word, are also slow growing and often multiple, and that tumors having their typical locality, even stainability, sometimes seem to appear concurrently with the carotid body-type group of tumors.[3] Furthermore, there surely exist true sympathetic paragangliomas without any chromaffin reaction. It seems that the chromaffinity of the cells is reached only in the final step of their differentiation. This is well demonstrated by the fact that not all cells in a pheochromocytoma are chromaffin.[9]

A special feature of the tumors described in the present case was the clearly distinct component consisting of primitive connective tissue. To the knowledge of the present authors such tissue has not been present in any tumors described previously. According to the literature, neurofibromatosis of the skin may coexist with a pheochromocytoma.[6, 19] We cannot definitely deny the presence of schwannomatous or neurofibromatous differentiation in some areas of the tumor removed in 1956. However, all the other features point to a true mesodermal type of growth. This again may have some bearing on the discussion concerning the histogenesis of tumors arising in carotid bodies and related structures. The view is expressed by some authors[2, 8] that tissue of mesodermal or vascular glomeral origin would be involved during their development. The structure of the two tumors in the present case seems to confirm this opinion. But also, the adrenals are, in the early embryogenesis, developed from two primitive anlagen, which for a long time remain separated. The cortical layer is mesodermal, the medulla ectodermal. Another suggestion is that perhaps a faulty organogenesis has something to do with the causal aspect of the tumors reported in this paper. Our knowledge is, however, too limited to warrant any conclusions applicable to these cases.

The necrotic foci, diminished organization of the tumor tissue, and the presence of mitotic figures and atypic cells in the tumor removed in 1956 were clear signs of a trend to malignancy as compared to the first tumor. Malignancy is rarely encountered in tumors of the parasympathetic system.[14] On the other hand, it is not as infrequent in the retroperitoneal tumors of a similar structure that are considered by Smetana[21] also to be nonchromaffin paraganglionic tumors. The signs of local malignancy in the latter tumor growing from diaphragmal tissue seem to be in keeping with the concept that malignancies are more common in the abdominal group of paraganglionic tumors than in the thoracocervical group.

In view of the variable features of the epitheloid tissue and of the adjacent richly vascularized connective tissue seen in the pathoanatomic examination of the first tumor, our case was first diagnosed as a malignant hemangioma. We refer in this connection to the first report of this case by Perasalo.[18] The new tumor which developed 5½ years later in the contralateral side of the thorax gave reason for reconsideration and re-analysis of the case.

SUMMARY

The authors describe two paraganglionic tumors developing in the thoracic cavity of a 56-year-old woman. The first tumor was fist-sized, was situated between the lobes of the left lung, and was adherent to the anterior mediastinum. The second tumor was excised 5½ years later because of the clinical

symptoms. It was adherent to the right hemidiaphragm and was of the size of a child's head. It showed signs of local malignancy. The size of both tumors was in large part due to a separate mesenchymal fibromyxomatous component. Recovery was uneventful after both surgical operations and the patient resumed her former occupation. The development of metastases has recently been suspected but in no way proved.

The authors discuss the classification of these tumors and suggest that the presence of small, sympathicogonia-like cells in the first removed nonchromaffin and carotid body-like tumor gives reason to associate both tumors closely with paragangliomas, in the original sense of the term. The finding of a primitive mesodermal component, in addition, was interesting in point of view of the histogenesis of paraganglionic tumors. The differentiation in principle of epitheloid structures associated with the sympathetic nervous system, on the one hand, and with the parasympathetic system, on the other hand, and of the tumors originating in these epitheloid structures does not appear to be well founded in all respects. The nonchromaffin portions of the tumors described in the present report are therefore merely termed paraganglionic.

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EMERGENCY PULMONARY RESECTION IN NECROTIZING PNEUMONIA

Thomas H. Hewlett, Lieutenant Colonel, MC, USA, Leland M. Bitner, Major, MC, USA,** and Patrick Moraca, Captain, MC, USA,****
Fort Sam Houston, Texas

INTRODUCTION

Emergency pulmonary resection during the course of an acute spreading infection within the lung is diametrically opposed to the established concept of deferring operation in acute pulmonary disease. Experience with acute necrotizing pneumonia of staphylococcic origin, which carries a prohibitive mortality of 75 to 80 per cent under intense medical treatment, stimulated the development of a combined medical-surgical approach to this disease and the utilization of emergency excision of diseased pulmonary tissue in these acutely ill patients.

The availability of sulfonamides and penicillin in 1952 led Sir Russell Brock[1] to predict that the mortality attributable to staphylococcic infection of the lungs would have to be revised downward. However, reports from the British medical literature of the past few years point out the persistence of a high mortality rate associated with the acute necrotizing pneumonia of staphylococcic origin. Fisher and his associates,[6] reporting on 21 cases of this type of staphylococcic pneumonia in adults, record a 66 per cent mortality despite intensive medical therapy. This is representative of the results currently being obtained in this country. Caswell and his colleagues,[2] reporting on the Temple University experience with antibiotic-resistant staphylococci, note the deaths of 3 out of 4 patients with bronchopneumonia treated with antibiotics to which the bacteria were susceptible. Regarding this entity, Caswell states, ''This mortality rate is precisely that reported in the presulfonamide preantibiotic era.''

Reports dealing with staphylococcic pneumonia in the French and German literature of 1889-1890 labeled it a complication of epidemic influenza.

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*Chief: Thoracic-Cardiovascular Surgery Service, Brooke Army Hospital, Fort Sam Houston, Texas.

**Chief: Communicable Disease Section, Brooke Army Hospital, Fort Sam Houston, Texas.

***Assistant Chief: Anesthesia Service, Brooke Army Hospital, Fort Sam Hosuton, Texas.

A classic description of the clinical picture of necrotizing pneumonia was published by Chickering and Park[3] in 1919 after observing an influenza epidemic in a military camp of World War I The fact that epidemic influenza may set the stage for staphylococcic pneumonia is well established, however, it can no longer be considered the sole predisposing factor Minor upper respiratory infection of an acute nature may pave the way for staphylococcic invasion of the bronchopulmonary tree Chronic bronchitis and varying degrees of pulmonary edema may establish a favorable environment for the growth of staphylococci in the respiratory tree of older or debilitated individuals A fatal staphylococcic process may develop as a superimposed infection in sites altered by pneumococcus pneumonia

Unfortunately, most reports have failed to differentiate clearly the several pathologic patterns of staphylococcic infection within the lung Consequently, the physician faced with an occasional case is confused by divergent mortality reports Brock's[1] 15 per cent mortality is applicable only to the abscess which can be expected to drain via bronchial routes The 69 to 90 per cent range applies specifically to the more virulent pattern

The initial insult of *Staphylococcus aureus* on pulmonary tissue is bacterial invasion of the bronchial mucosa which produces a peribronchial zone of *hyperemia in which minute foci of consolidation appear* These foci rapidly progress to miliary type abscesses The individual response to the infection differs in the infant and adult age groups

The picture established within the infant lung usually falls into one of three categories (a) the peribronchial reaction may tend to remain localized, producing a check valve effect on the bronchioles resulting in the trapping of air in the distal alveoli with the subsequent development of one or several pneumatoceles, (b) the peribronchial miliary abscesses may rapidly extend to perforate the visceral pleura producing pneumothorax and empyema, and (c) a and b may develop simultaneously in the same infant

In the adult lung there may occur a lobular bronchopneumonia Scattered small areas of parenchymal infiltration occur which tend to disappear *when the patient can effectively clear the tracheobronchial tree* This may be unrecognized unless frequent x-ray studies are carried out and bacteriologic studies performed routinely This pattern may be self limiting or progress to the more severe types, possibly by bronchial embolization

Second a localized abscess may occur The minute abscesses may become confluent to produce a sharply localized area of necrosis in close proximity to a bronchus This area may be evacuated spontaneously via a bronchus leaving a temporary cystlike space resembling a pneumatocele Parenchymal destruction may be minimal and complete healing takes place Such a process may, in its healing, leave a dense parenchymal fibrosis or localized bronchiectasis

Localized abscesses in the periphery of the lung may perforate the visceral pleura and produce a bronchopleural fistula with empyema early in the course of the disease Such a pattern might be anticipated when the initial process is developed in the middle and lower lung fields. The pleural response to the development of a bronchopleural fistula is the rapid formation of a dense, trapping peel.

Third, there may occur a necrotizing pneumonia. The peribronchial abscesses become confluent to produce a coalescence of the bronchial mucosa and alveoli. The segment or lobe is totally involved in a hemorrhagic necrosis and the bronchi are occluded with necrotic slough. The zone of the lung is airless. It occupies its normal space as a solid edematous mass. The visceral pleural reaction is limited to a fibrinous exudate without the development of significant effusion. This process spreads locally by direct contiguity and is no respecter of fissures. The rapid progress of this process suggests that there is early impairment of the bronchial circulation within the lobe, resulting in tissue death. The pulmonary circulation within this area immediately becomes a useless shunt, and total disintegration of the involved lobe ensues. The spread to the contralateral lung is usually by bronchial embolization. The radiographic density exhibited by such tissue is frequently misinterpreted as pleural effusion.

It is readily appreciated that drainage is an essential feature in the types of the disease which exhibit a tendency to recover on conservative management. Necrotizing pneumonia is an unsolved problem and the following case reports serve to demonstrate a new approach which offers promise. Four patients subjected to emergency pulmonary resection during the acute phase of necrotizing pneumonia are presented.

CASE REPORTS

CASE 1.—(Figs. 1-6) A white army nurse, 41 years of age, was admitted to the hospital complaining of right anterior chest pain and fever. The patient had been treating herself for a cold for approximately 3 weeks with antipyretics and oral antibiotics. Ten days prior to admission, pharyngitis and rhinorrhea had become marked and during this period her temperature had risen daily to 102° F. The past history disclosed a lobar pneumonia in 1941, and viral pneumonia in 1948. The patient had had a recent 8 months' tour of duty in Indo-China.

Physical examination revealed a temperature of 101.8° F., pulse 96, and blood pressure 116/64. This patient appeared undernourished and acutely ill. The pharynx was mildly injected. Auscultation of the chest revealed harsh breath sounds bilaterally; there were no localized râles or areas of dullness. The abdomen was negative. Laboratory examination disclosed a white cell count of 15,000 with 80 per cent neutrophils. A throat culture yielded *Diplococcus pneumoniae*. X-ray studies showed infiltration limited to the right middle lobe.

The following therapeutic regimen was instituted on admission: penicillin 40 million units daily, streptomycin 2 Gm. daily, Achromycin 2 Gm. daily, intermittent positive pressure, and Alevaire and Isuprel every 2 hours. Postural drainage of the middle lobe was attempted. The patient showed no response to a 10-day course of this treatment. Temperature fluctuated between 102° and 103° F. Bronchoscopic examination performed on the twelfth hospital day showed the right middle lobe bronchus to be displaced downward and occluded with thick tenacious mucus. Repeated aspiration via the bronchoscope was ineffective. Throughout the hospital course, the roentgenograms revealed persistence of the middle lobe consolidation. Coughing and positive pressure breathing were ineffective in producing significant amounts of sputum. By the fifteenth hospital day the temperature had stabilized at 104° F.

On the twenty-third day, an emergency middle lobectomy was carried out under endotracheal cyclopropane-ether anesthesia. The middle lobe occupied its normal space; its pleural

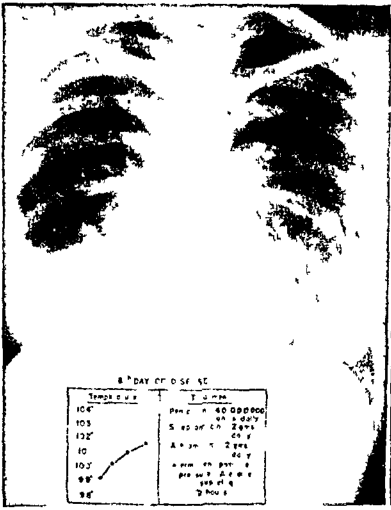


Fig 1

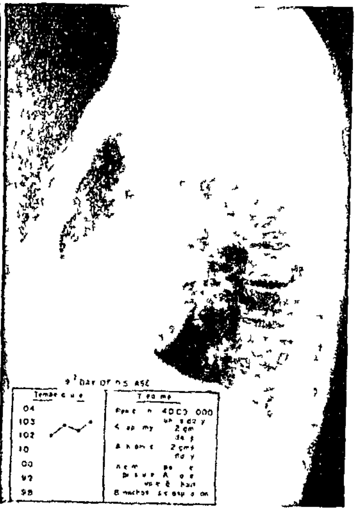


Fig 2

Fig 1.—Case 1 Right middle lobe infiltration
Fig 2.—Case 1 Persistence of middle lobe process despite treatment

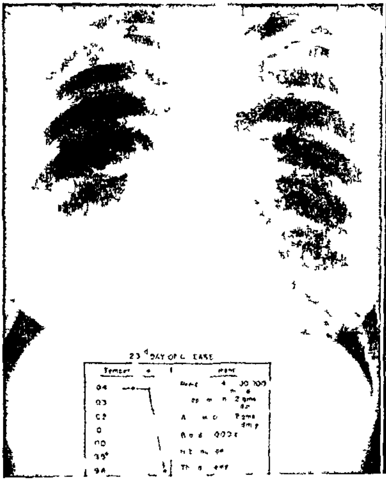


Fig 3

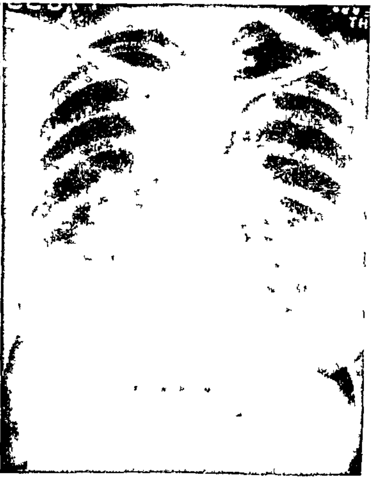
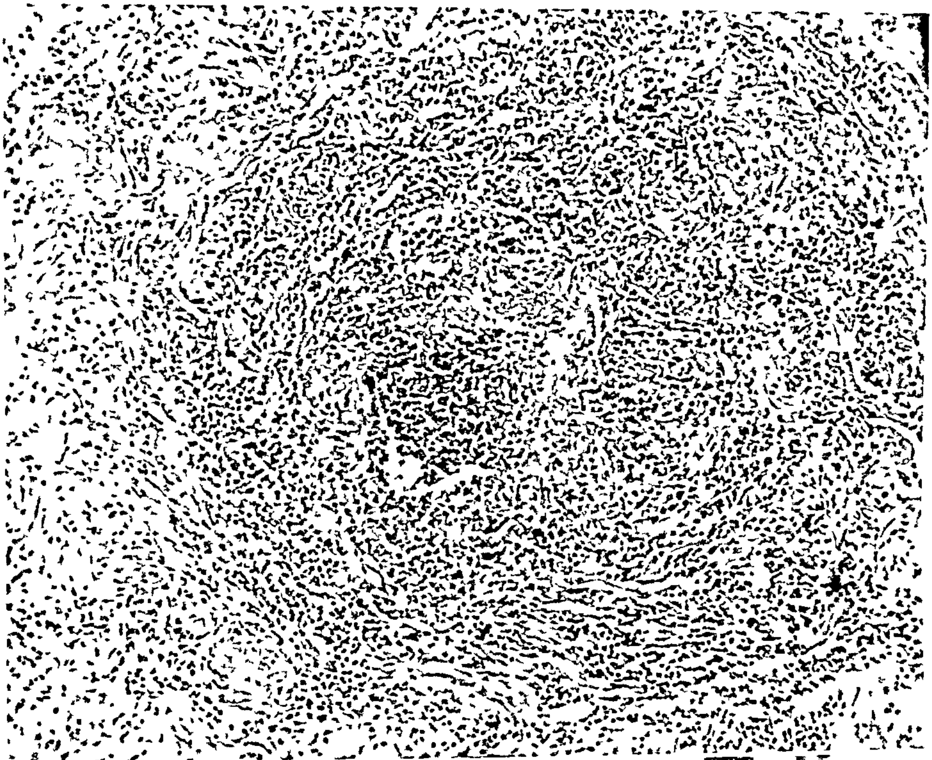


Fig 4

Fig 3.—Case 1 Preoperative film
Fig 4.—Case 1 After middle lobectomy—function studies normal

Fig. 5.



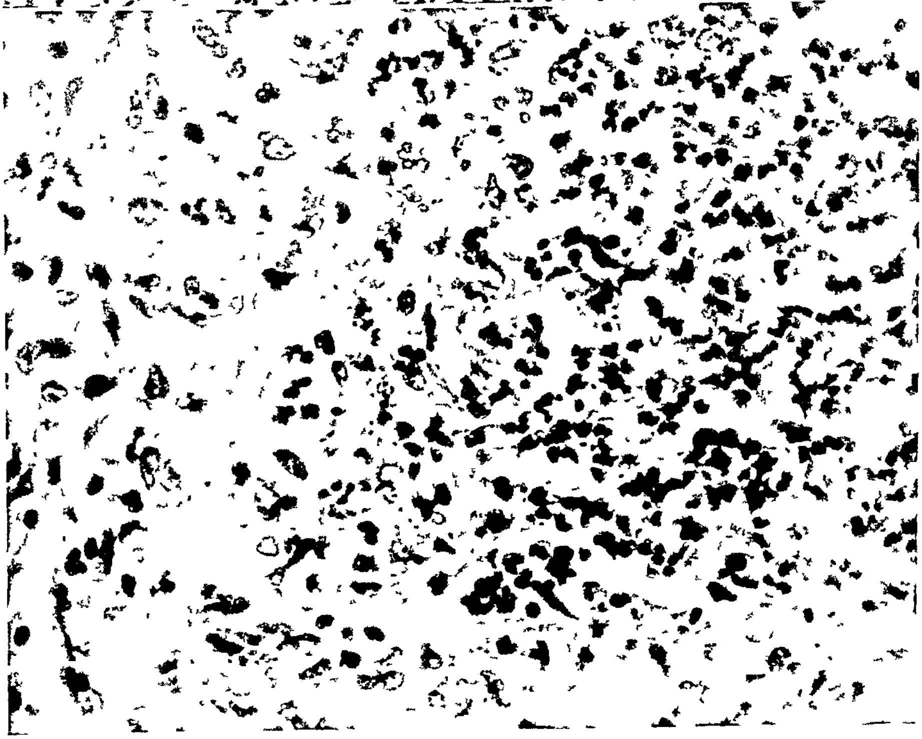


Fig 6

Fig 5.—Case 1. Microscopic section (×105)
Fig 6.—Case 1 Microscopic section (×475)

surface was covered with a shaggy plastic exudate On palpation, the lobe had a rocklike consistency The inflammatory process had not crossed fissure lines Hyperemic edematous glands were prominent in both fissures and about the middle lobe bronchus The middle lobe bronchus was edematous and friable at the point of transection On section of the specimen total destruction of the architecture was noted Multiple minute granulomas were scattered throughout the lobe At completion of the operation, the patient's temperature which had been 104° F on arrival in the operating room was recorded at 98 9° F

The clinical course showed dramatic improvement following operation The temperature did not exceed 100° F despite the development of a bronchopleural fistula This fistula closed spontaneously The patient underwent decortication 6 weeks after lobectomy Recovery from the second operation was uneventful and pulmonary function studies were within normal limits

Pathologic Examination —

Gross The serosal surface of the lung showed areas of hemorrhage and fibrous adhesions Multiple sections through the lung revealed innumerable whitish discrete nodules which averaged 1 to 2 mm in diameter These nodules became confluent in some areas The gross appearance suggested an active granulomatous process Typical lung abscess was not encountered during gross examination

Microscopic All sections examined presented the same picture There were numerous discrete granulomas filled with neutrophils surrounded by an inflammatory granulation exhibiting early fibrosis Broad zones of organizing pneumonia separated the granulomas Focal and diffuse areas of necrosis and pneumonitis involved the alveolar walls and septae Exudate was composed of fluid fibrin and mononuclear cells As the reaction was seen throughout the pulmonary parenchyma it probably represented a specific type of infection The over all findings were those of suppurative organizing bronchopneumonia Bacteria were not demonstrated by special staining techniques

Comment —Repeated sputum cultures and cultures of bronchoscopic washings failed to disclose the etiology of this process Likewise, cultures of the resected lobe were negative, however, clinically, this patient's course was consistent with the staphylococcic process The microscopic examination of the resected tissue suggested that the process was halted in the course of its progress toward a true necrotizing pneumonia At no time did the patient exhibit findings consistent with true abscess formation The prompt clinical response to lobectomy in this patient indicated that emergency resection might be useful in the management of certain acute pulmonary infections which did not drain via normal routes and which exhibited no tendency to improve on adequate medical therapy Bronchopleural fistula is to be anticipated as a complication due to the local disease process within the bronchial wall

CASE 2 —(Figs 7 12) A 22 year old white man was admitted to Brooke Army Hospital by transfer from another hospital This soldier returned to this country from Germany on Sept 21, 1957, at which time he was suffering from a cold characterized by a dry hacking cough During October the cough increased and became productive of blood tinged sputum throughout this period outpatient treatment had been ineffective He was hospitalized November 4

Chest roentgenogram at this time revealed a small area of infiltration in the left lower lobe Achromycin, 2 Gm daily, Alevaire and Isuprel inhalations and expectorants comprised the hospital treatment and for the next 15 days his temperature ranged from 100° F to 103° F His clinical condition gradually deteriorated, although his temperature stabilized at lower levels, 99° to 100° F Roentgenograms of the chest revealed a slow increase in the area of infiltration in the left lower lobe Sputum cultures during this hospital period yielded hemolytic *Staphylococcus aureus* and streptococcus The cough progressed to become productive of mucopurulent sputum There was a 6 pound weight loss Skin tests were reported as follows purified protein derivative No 2 positive, histoplasmosis and coccidioidomycosis, negative White blood cell count during this month of hospitalization varied from 12,000 to 12,800

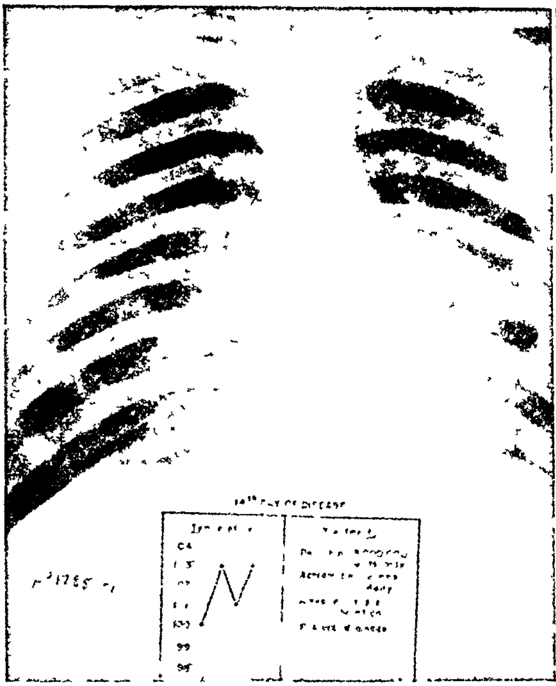


Fig. 7.

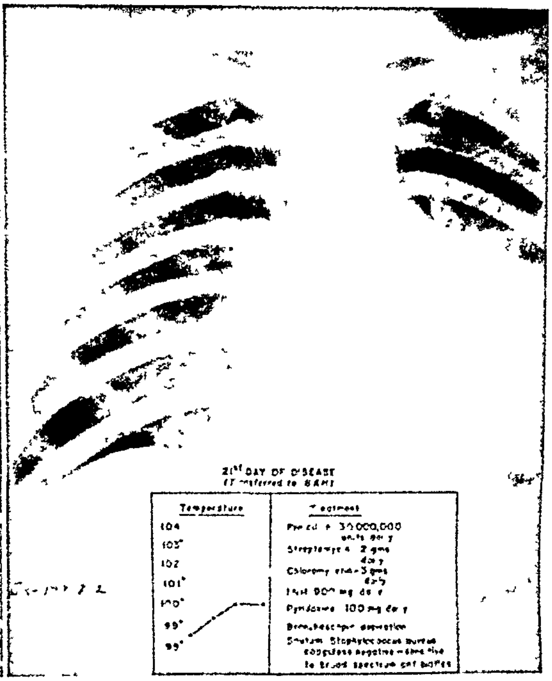


Fig 8.

Fig. 7.—Case 2. Initial x-ray findings.
Fig. 8.—Case 2. Progressive parenchymal infiltration of left lower lobe.

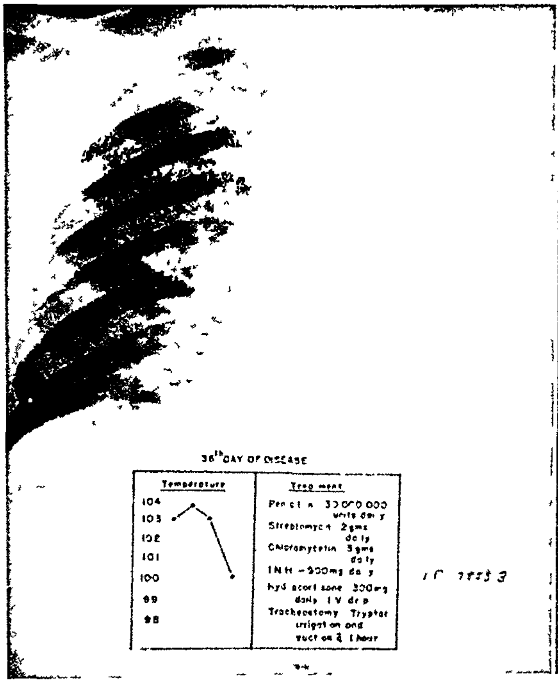

36th DAY OF DISEASE
Temperature
104
103
102
101
100
99
98
Treatment
Penicillin 30,000,000 units daily
Streptomycin 2 gms daily
Chloromycetin 3 gms daily
INH—300 mg daily
hydrocortisone 300 mg daily I V drip
Tracheostomy Tryptar irrigation and suction ¼ 1 hour

Fig 9.

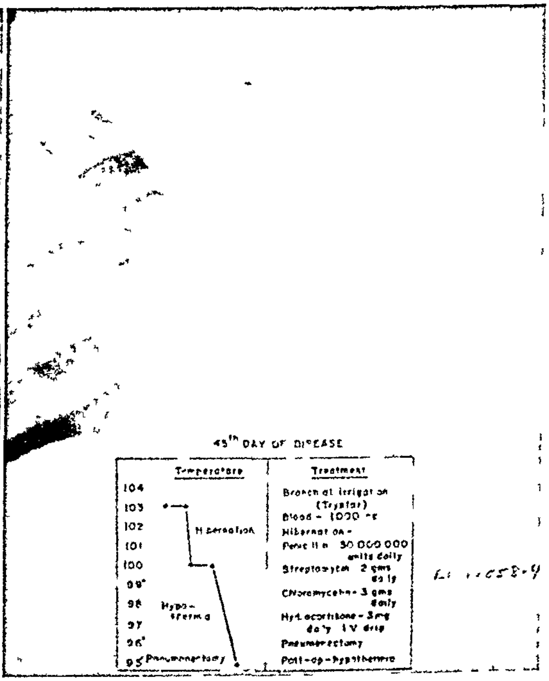


Fig. 10.

Fig. 9.—Case 2. Progressive parenchymal destruction. No pleural fluid.
Fig. 10.—Case 2 Total destruction of left lung with spread to right upper lobe.

This patient was transferred to Brooke Army Hospital on the thirty-ninth day of his disease. Physical examination revealed an acutely ill, mildly lethargic, young man. Temperature was 104° F., pulse 120, respirations 32, and blood pressure 138/88. The left hemithorax was splinted and dull to percussion. No breath sounds were heard over the left lung. The *pharynx was hyperemic. The abdomen was negative Sputum culture yielded Staphylococcus aureus,* coagulase negative, sensitive to broad spectrum antibiotics

The following therapy was instituted on admission: daily, by intravenous route, penicillin 20 million units, streptomycin 2 Gm., Chloromycetin 3 Gm.; oral medication—isonicotinic acid hydrazide 400 mg., and pyridoxine 150 mg. On the forty second day of disease, the patient's temperature ranged upward to 106° F. Bronchoscopy revealed an exuberant granulation process occupying the major portion of the left main stem bronchus. *Thick, anchovy-like pus was removed from this site with a biopsy forceps. Following this,* there was suggestive evidence of return of aeration to the left upper lobe. Digitalization was accomplished. Bronchoscopy with removal of large amounts of pus was performed several times on the forty fifth day of disease. Left thoracentesis yielded 50 c.c. of serosanguineous fluid. Emergency thoracotomy was proposed at this time, but it was postponed hoping that further clearing of the left upper lobe would obviate pneumonectomy. On the fiftieth day of disease, the patient's temperature was lowered by continuous intravenous drip of hydrocortisone 300 mg. daily. Low hemoglobin was corrected with three units of blood. The patient seemed to stabilize for a period of 9 days during which time bronchoscopic aspiration and irrigation were performed daily. White cell count was 18,300, neutrophils 94, lymphocytes 6, and hemoglobin 9.6. However, on December 17, the sixty-sixth day of disease, the temperature started to ascend. Tracheostomy was performed and aerosal tryptar was instituted every 2 hours. Copious amounts of thick pus were aspirated from the tracheostomy tube. *On December 18, x-ray studies revealed total consolidation of the left lung with an* infiltrative process in the upper lobe of the right lung.

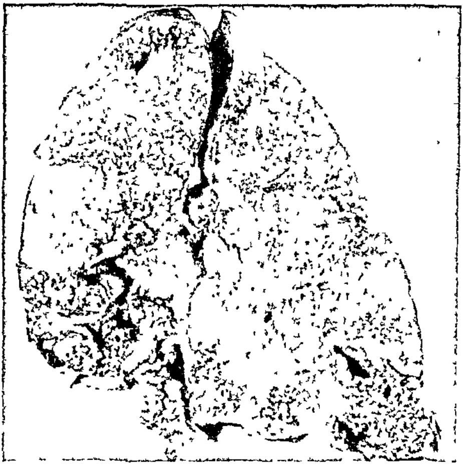


Fig. 11.—Case 2. Gross specimen of left lung.

On the seventieth day of disease, white cell count was 32,900, neutrophils 94, lymphocytes 6, and hemoglobin 10 4 Gm. Artificial hibernation was begun and the patient's temperature was reduced to 95° F. by surface cooling with Thermorite blankets. A left pneumonectomy was performed. The left lung was free of adhesions, the pleural surface was covered with a thin shaggy exudate and there was no intrapleural fluid. The lung was firm and edematous, its surface presenting transverse imprints of the adjacent ribs. Pulmonary vessels were ligated and divided within the pericardium as their exposure within the hilus was technically impossible. The pericardial sac contained grayish, cloudy fluid. The mainstem bronchus was necrotic in its zone of division near the carina. Extraction of the intact specimen could not be carried out through the routine posterolateral incision, consequently, it was fragmented during extraction of the specimen from the pleural cavity. Section of the resected lung revealed total destruction of the parenchyma. Artificial hibernation was maintained and patient's temperature was controlled to a level of 97° F. until he died 17 hours after operation.

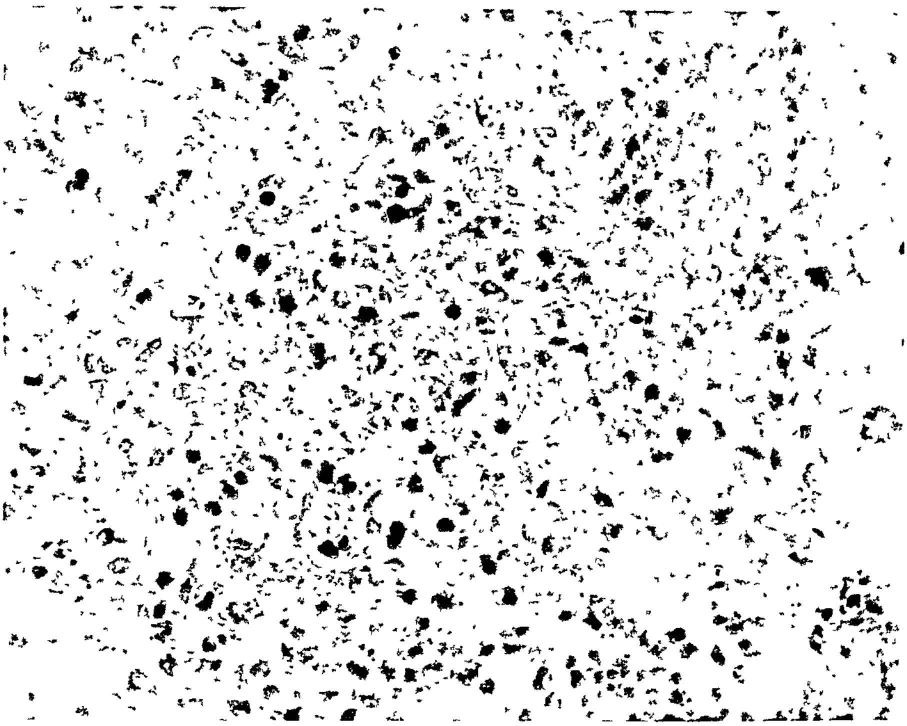


Fig. 12.—Case 2. Microscopic section (×475).

Pathologic Examination.—

Gross: The left lung was completely consolidated except for a small partially aerated portion of the upper lobe. The pleural surface of the lung was white in color with scattered patches of exudate. No areas of adhesions were noted.

Microscopic: There was diffuse suppurative bronchitis with obstruction and ulceration of the bronchial mucosa. Pulmonary parenchyma showed diffuse necrosis with organization of a suppurative bronchopneumonia. In some areas there were broad sheets of fibrinoid-like material with thickened alveolar septa, with organization of bronchial secretion and complete consolidation of focal areas within the lung parenchyma. Several areas showed confluent abscess formation especially around small- and medium-sized bronchi. Diagnosis: pneumonitis; diffuse consolidation and organization; suppuration and confluent abscesses.

Comment.—The unrelenting progression of disease was well illustrated in this instance. In retrospect, it is likely that this patient would have survived if he had undergone thoracotomy when it was first proposed. Even at that time, left pneumonectomy would probably have been the operation of choice. Desperation pneumonectomy in the face of contralateral disease is not advocated as it offers no promise of significant reduction in the existing mortality rate.

CASE 3.—(Figs. 13-18.) A 39-year-old Negro woman was hospitalized with complaint of suboccipital headache, rhinitis, right chest pain, and blood-streaked sputum. Her general health had been good until 3 days prior to admission when a cold became complicated by marked nasal discharge and headache, cough had increased in frequency and severity, and slight blood streaking of the sputum had been noted for 24 hours. Physical examination disclosed an acutely ill female with a temperature of 102° F., pulse 100, respirations 24, blood pressure 118/90, and grunting respiratory distress. The nose and throat were moderately hyperemic. The right thorax was splinted, and rhonchi and wheezes were present throughout the right chest. Percussion note was slightly impaired in the right lower chest. The abdomen was negative except for bilateral adnexal tenderness. Skin tests of purified protein derivative, coccidioidin, and histoplasmin were negative. Laboratory examinations revealed a white cell count at 18,000, neutrophils 80, lymphocytes 16, and a hemoglobin of 12 Gm. Sputum smear showed gram-positive cocci. On December 22, a sputum culture yielded *Staphylococcus aureus* coagulase positive, sensitive to Chloromycetin. The temperature varied between 101° and 103° F. During this period, she received penicillin, 2 million units, and streptomycin, 2 Gm. twice daily. Following the recovery of *Staphylococcus aureus* from the sputum cultures, the treatment was changed to the following: chloramphenicol 3 grams, penicillin 60 million units, tetracycline, 750 mg., and streptomycin 2 Gm. daily, by continuous intravenous drip. Hydrocortisone, 300 mg. daily, was started. Chest roentgenograms on the sixth day of disease were interpreted as revealing the presence of pleural fluid. Thoracentesis failed to confirm this. On the seventh and eighth days, the patient's temperature remained at lower levels, and she was symptomatically improved. Râles and dullness persisted over the right base. Chest x-ray studies were consistent with progression of the infiltrative process in the right lower lobe. The patient's clinical course deteriorated rapidly on the ninth day. Temperature rose to 102° F., pulse 120, and respirations 38. Sputum production was minimal. White cell count was 32,500 with 88 per cent neutrophils. Antibiotics were changed to the following, administered by continuous intravenous drip: penicillin 105 million units, ristocetin 3 Gm., Chloromycetin 3 Gm., streptomycin 3 Gm., and erythromycin 3 Gm.

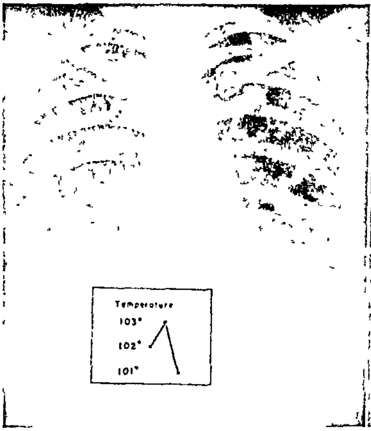


Fig. 13

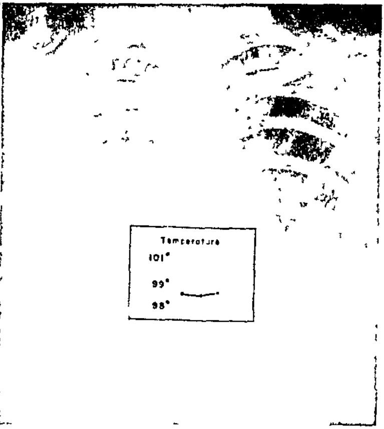


Fig. 14.

Fig. 13.—Case 3. Third day of disease—infiltration of right lower lobe.

Fig. 14.—Case 3. Sixth day of disease—spread of disease under therapy No pleural fluid

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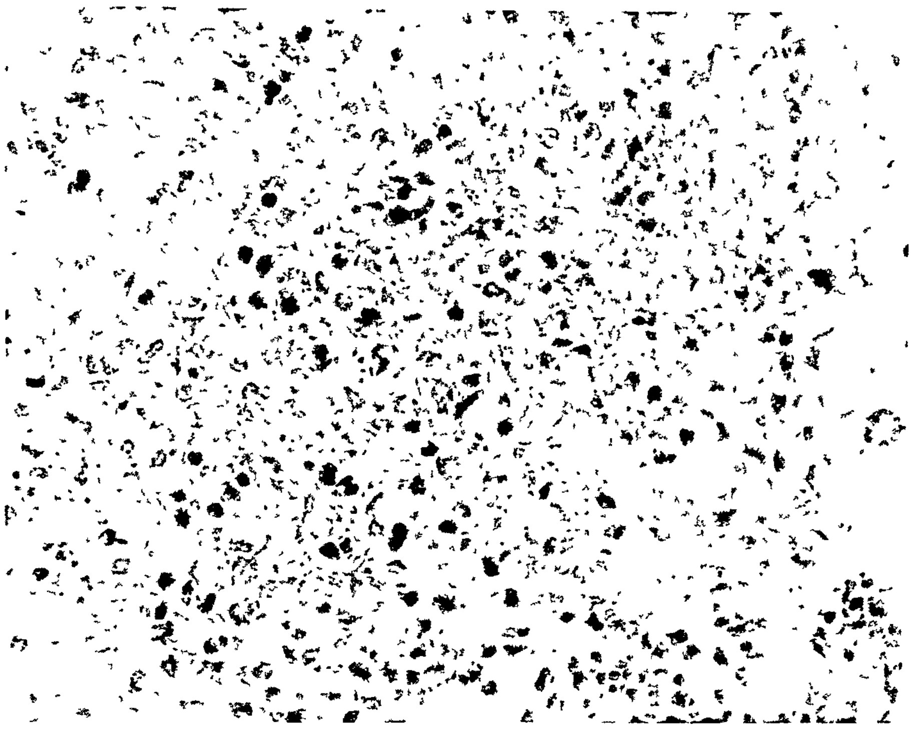

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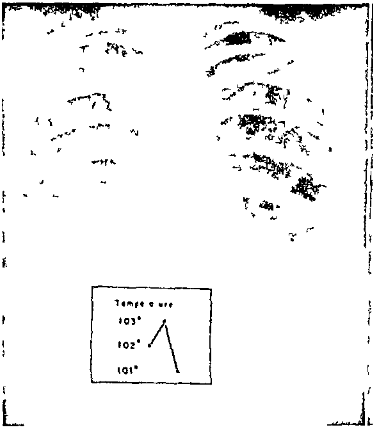

Fig. 13

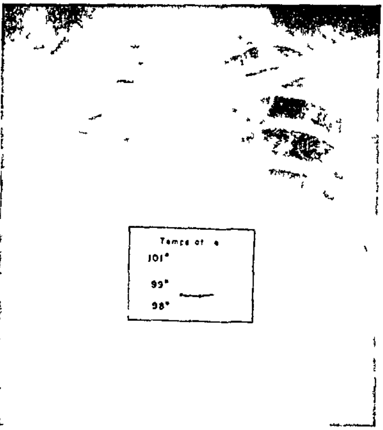

Fig. 14

Fig. 13.—Case 3. Third day of disease—infiltration of right lower lobe.

Fig. 14.—Case 3. Sixth day of disease—spread of disease under therapy. No pleural fluid.

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The patient continued to deteriorate clinically and right thoracotomy was deemed essential. Artificial hibernation was instituted. The patient was cooled to 94.5° F. with aid of Thermorite blankets. Right thoracotomy was performed. The necrotic process was found to involve only the lower lobe. Routine lower lobectomy was carried out.

Postoperatively, the patient was greatly improved; drug therapy was continued. Her temperature was controlled to a normal level by continued hibernation and hypothermia for 48 hours postoperatively. Following discontinuation of hibernation, temperature reached 100° F. on two occasions. All antibiotics were discontinued on the sixteenth postoperative day. Thoracotomy tubes were removed after 72 hours. The recovery was uneventful and patient resumed normal activity 30 days after onset of illness.

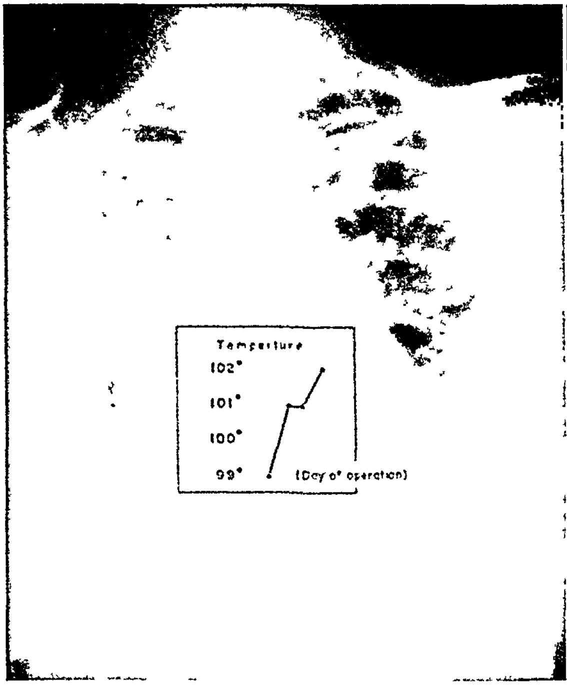


Fig 15.

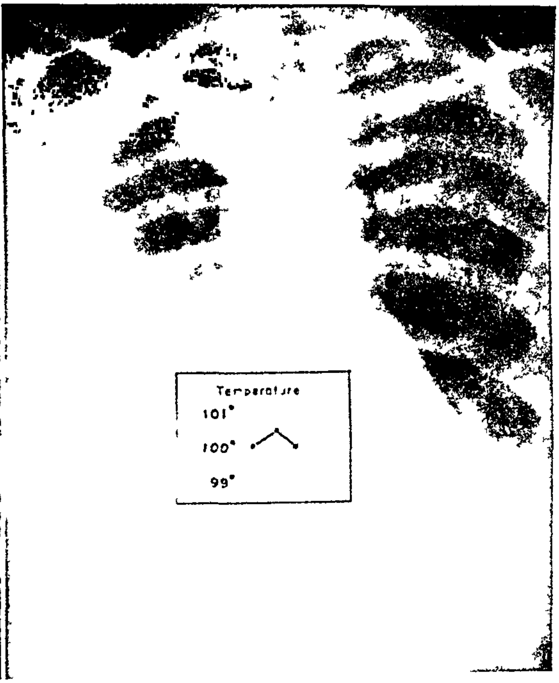


Fig 16

Fig 15.—Case 3 Ninth day of disease—day of operation.
Fig 16.—Case 3. Third postoperative day.

Pathologic Examination.—

Microscopic: The bronchi were all similar; there appeared to be hyperplasia of the bronchial epithelium. It was thick, dense, and piled in some areas; in other areas there appeared to be actual ulceration and erosion of the bronchial mucosa. Some of the bronchi were large, distended, and filled with mucopurulent exudate. The exudate extended into the smaller and terminal bronchioles. The pulmonary parenchyma showed a diffuse consolidation with marked thickening of alveolar septa and infiltration with inflammatory cells. In other areas the pulmonary parenchyma showed large and small abscesses with necrotic degenerating centers. In some areas, there was coalescence of the individual abscesses. Precipitated proteinaceous material and fibroblasts along with the collapsed alveoli made almost a solid mass of pulmonary parenchyma in the areas adjacent to the multiple abscess. In some areas the abscessed cavities and abscessed walls extended out to the visceral pleura.

Comment.—The clinical course of the disease and the radiologic findings illustrated our indications for the use of excisional surgery. After 72 hours of treatment, the patient's temperature appeared to be controlled, and she was somewhat improved clinically; however,

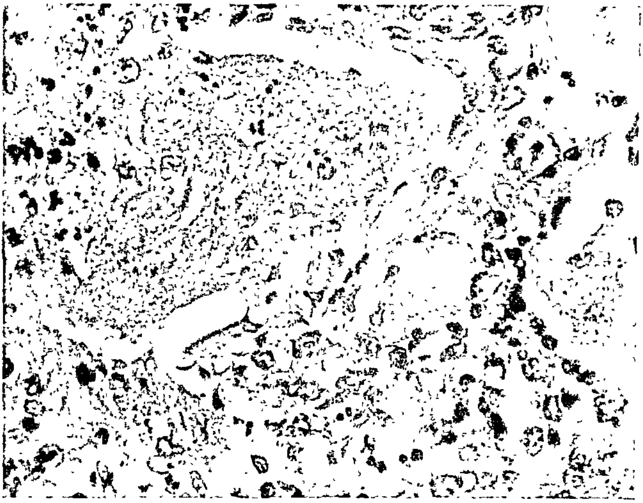


Fig. 17.—Case 3. Microscopic section (×475).

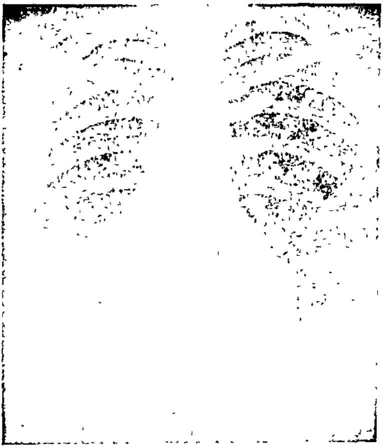


Fig. 18.—Case 3. Follow-up film.

x-ray studies showed marked progression of the right lower lobe infiltration. By the ninth day of her illness, despite continued antimicrobial therapy, she began to manifest evidence of rapid clinical deterioration with further x-ray evidence of increase in the pulmonary infiltration. Right lower lobectomy was performed, utilizing the artificial hibernation-hypothermia technique. Following discontinuance of this support on the third postoperative day, the patient did not become hyperthermic; 100.4° F. was the highest temperature noted in the postoperative period. Her postoperative clinical course demonstrated that properly timed surgical intervention in these patients can produce a satisfactory result. The destruction evident in this resected lobe was such that had she been fortunate enough to survive the acute disease the damaged residual lung would have necessitated an operation and additional hospital care.

CASE 4.—(Figs. 19-26.) This 36-year-old man was admitted to Brooke Army Hospital on May 29 because of dyspnea, fever, and left chest pain. About mid-May, this patient had been treated for a 2-day bout of cramping abdominal pain. This was complicated by swelling of the ankles. One week prior to admission to Brooke Army Hospital a cough developed with left anterior chest pain. This progressed to a cough productive of blood-streaked mucopurulent material, persistent fever, and increasing weakness.

Physical examination disclosed a cyanotic patient in acute respiratory distress, temperature 101° F., respirations 40. The pharynx was injected. There was limited expansion of the chest on the left; intercostal retraction was noted on the left. Breath sounds were decreased in the left hemithorax, and coarse rhonchi and râles were heard over the left lung. The abdomen was negative. The extremities showed pitting edema. Laboratory examinations revealed the white cell count to be 15,850 with neutrophils 90, lymphocytes 10. Hemoglobin was 10.6 Gm., hematocrit 34, serum sodium 138, serum chlorides 97, potassium 4, blood urea nitrogen, 29.5 mg. per cent, and CO_2 18 mEq. per liter. Urine showed a specific gravity of 1.025, sugar 2+ positive, albumin negative. A smear of the pleural exudate showed gram-positive cocci, and gram-negative diplococci. This patient was practically moribund on arrival in the ward. Pulse and blood pressure were not obtained.

Tracheostomy was performed without anesthesia. Aspiration yielded copious amounts of foul-smelling, yellowish pus. A similar material (1,500 c.c.) was removed by left thoracentesis. The cyanosis cleared rapidly. After 2 hours of Levophed support, the blood pressure stabilized at 130/80, pulse 110, and respirations 20. The Levophed was discontinued. A mushroom catheter was inserted into the left pleural cavity via the eighth interspace and attached to water-seal drainage. Bronchoscopy and tracheobronchial lavage resulted in further clearing of the airway. Digitalization was accomplished with intravenous Cedilanid. The thoracotomy tube ceased to function after 48 hours; the position was corrected and 300 c.c. of pus drained promptly. Atelectasis of the left lower lobe persisted despite bronchoscopy and repeated tracheal suction. A total of 1,000 c.c. of blood was given. The patient appeared confused and irrational. On June 2, a second thoracotomy tube was inserted and 1,200 c.c. of pus was evacuated from the left pleural cavity. His mental state improved steadily until June 5.

On June 6, the patient was extremely toxic; drainage via the thoracotomy tubes was poor. Blood (1,000 c.c.) was administered, hydrocortisone (100 mg.) was given and, under hibernation hypothermia, a left lower lobectomy was performed. Culture of the fluid exudate yielded microaerophilic streptococcus and *Staphylococcus albus,* coagulase negative, sensitive to chloramphenicol, oxytetracycline, and streptomycin. At operation, several large loculated empyema pockets separated by old pleural adhesions were encountered with necrosis of pulmonary tissue involving the posterior segment and superior division. Considerable intractable oozing was encountered in the region of the pulmonary ligament and from the parietal pleural surface. The upper lobe inflated easily and appeared free of parenchymal disease. Pleural drainage was established with two large rubber tubes.

During the first 24 hours postoperatively, the patient continued to ooze to the point of collapse of the left upper lobe, and production of a mediastinal shift A second operation was carried out June 7 which revealed bleeding from the chest wall and in the area of the pulmonary ligament This was controlled with electrocautery and Gelfoam sutured into the bleeding sites The left upper lobe was re expanded and suction applied to the thoracotomy tubes Following the second operation the patient received adequate blood transfusions and was maintained with a Bennett respirator for 36 hours All drugs were discontinued by June 14 On June 20, he received pneumoperitoneum to aid in the closure of the bronchopleural fistula The residual bronchopleural fistula was treated by open thoracotomy tube until the pleural space was reduced to a 10 c c capacity

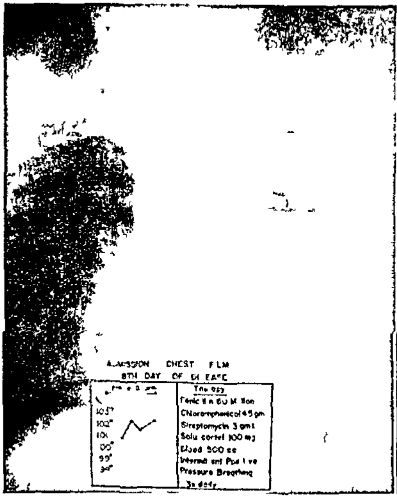


Fig 19

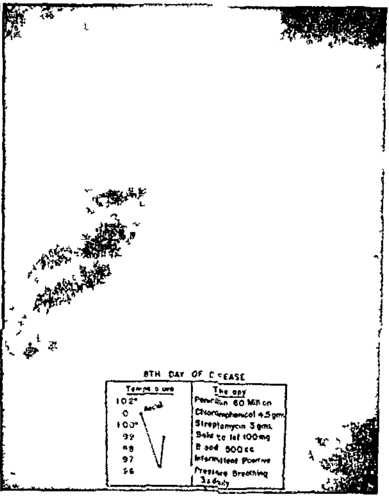


Fig 20

Fig 19 —Case 4 Massive pyopneumothorax
Fig 20 —Case 4 Following tracheotomy and thoracostomy drainage

Pathologic Examination —

Gross The lower lobe of the lung was firm, the pleural surface markedly thickened Sectioning revealed two large abscess cavities The diameter of one of the cavities measured 3 cm A large abscess near the pleural surface measured 6 cm in diameter

Microscopic Sections from various portions of the lobe were similar The picture was that of an acute inflammatory abscess with an abundance of neutrophils and necrotic debris in the central portion No fibrous encapsulation was noted There was increased fibrin deposit about the rim of the abscess The surrounding lung was frequently collapsed and focal areas of scarring were noted

Comment —The disease pattern exhibited by this patient appears to have been due to a fulminating staphylococcic infection occurring within a previously damaged lobe of the left lung with early drainage into areas of pre existing chronic pleuritis The resultant empyema drained via the bronchus almost causing asphyxiation of the patient. The decision for

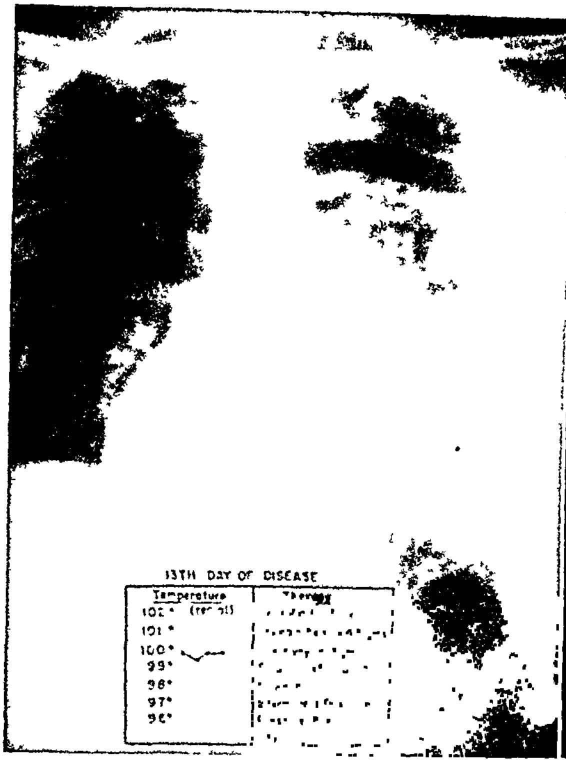


Fig 21.

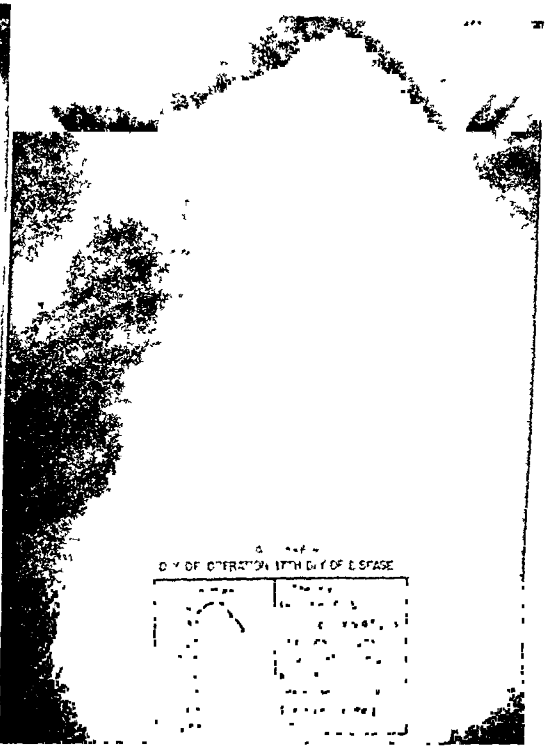


Fig. 22

Fig 21.—Case 4. Following use of multiple thoracotomy tubes
Fig. 22.—Case 4. Beginning of postoperative hemothorax.

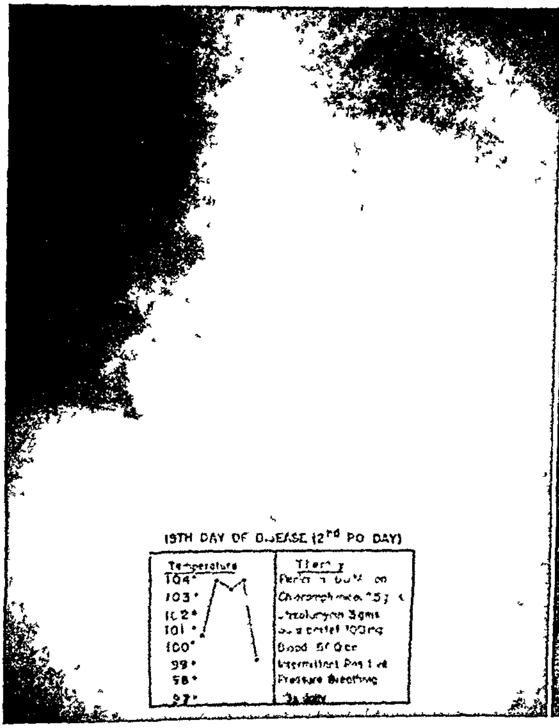


Fig. 23.

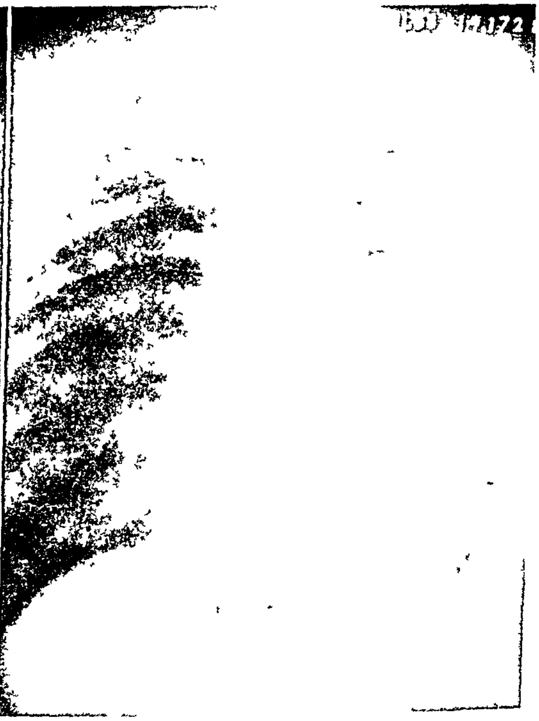
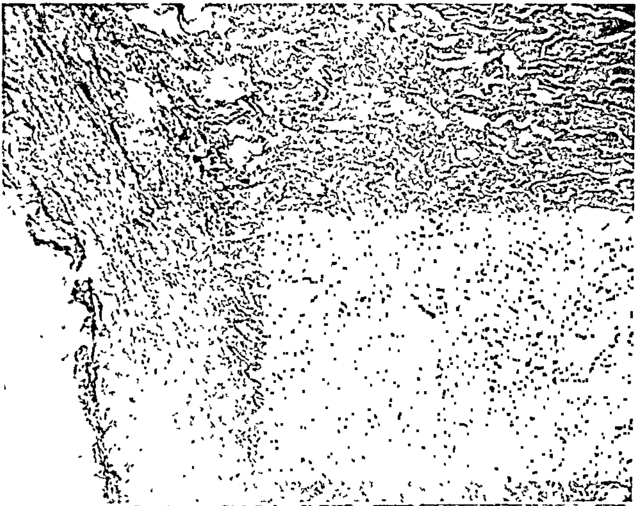


Fig 24.

Fig. 23.—Case 4. Stabilization following second thoracotomy for hemothorax
Fig. 24.—Case 4. Follow-up film—twenty-fifth postoperative day.

Fig 25



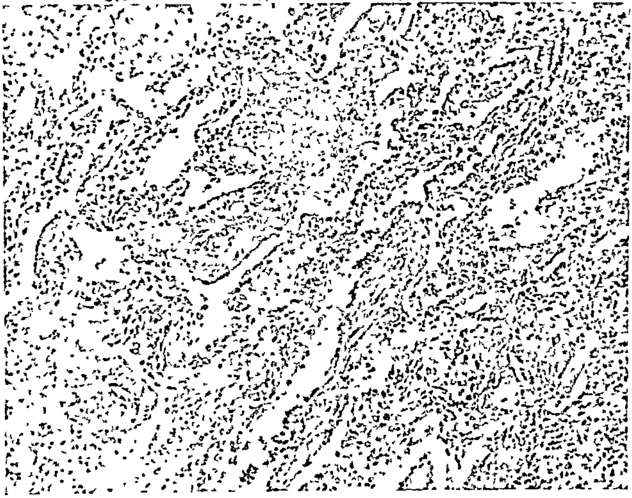


Fig. 26.

Fig. 25.—Case 4. Microscopic section (×30).
Fig. 26.—Case 4 Microscopic section (×105).

emergency surgical intervention was based on the clinical deterioration and the failure of multiple thoracotomy tubes to drain the empyema effectively. The complication of continued postoperative bleeding, necessitating a second thoracotomy, was attributable to the extensive old pleuritis in this patient. The bronchopleural fistula was anticipated following suture of a bronchial stump which showed signs of early necrosis. Both complications responded readily to proper therapy indicating that the acute process had been brought under control as a result of lobectomy.

DISCUSSION

Minor surgical techniques have long been utilized as a supplement to the medical treatment in the less virulent types of staphylococcic infection within the lung. The efficacy of closed intercostal tube drainage in infants who develop tension pneumothorax or pyopneumothorax is well known. Clinical improvement is usually prompt when such drainage is instituted. The early development of empyema in the adult requires similar drainage of the pleural space before control of the infection is attained.

Patients who survive staphylococcic infection of the lung, under conservative medical treatment, do so only because their individual response to the infection includes drainage via the tracheobronchial tree or via the pleural cavity. A significant percentage of adults surviving the acute stage of the disease require operation to remove crippling bronchiectasis and extensive fibrosis.

The necessity for drainage of staphylococcic infections throughout the body has not been negated by the development of antimicrobials. Effective drainage does not occur in necrotizing pneumonia for several reasons. Normal ciliary reflexes of the bronchial mucosa are lost because of widespread destruction in the bronchial wall. The gelatinous necrotic debris that collects in the bronchi serves as a mechanical block. The accompanying toxemia quickly exhausts the patient so that cough is ineffective. A vicious cycle is thus developed and tissue destruction continues unabated. The impaired circulation to the local area prevents antibiotics from reaching the infected site. The futility of medical treatment in such a situation is more apparent when it is realized that "in vitro" sensitivity of the staphylococcus to specific antibiotics is not proof positive of "in vivo" response.

The idea of emergency pulmonary resection herein proposed is new in this country yet it is not without precedent. Sellors and his colleagues[12] reported, in 1946, a series of patients suffering with spreading pneumonitis. They noted the prospect of cure with conservative measures to be less than 20 per cent. In their experience, emergency pulmonary resection resulted in a significant salvage not previously obtained. We were not aware of this report prior to using emergency resection on the patients reported here.

The complication rate associated with emergency pulmonary resection in acute necrotizing pneumonia, although somewhat higher than that associated with resection in advanced bronchiectasis, is of little significance when considered in relation to the marked reduction in mortality which appears possible.

Further evaluation of emergency pulmonary resection in fulminating necrotizing pneumonias seems warranted

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STUDIES OF PULMONARY FUNCTION BEFORE AND AFTER PULMONARY SURGERY IN 450 TUBERCULOUS PATIENTS

I. Vital Capacity and Maximum Breathing Capacity

John K. Curtis, M.D., Helene Bauer, A.B., Howard K. Rasmussen, B.S.,
and John T. Mendenhall, M.D., Madison, Wis.

PULMONARY resection of residual lesions larger than 1 cm. in size and the removal of persistent cavities have become standard procedures in many hospitals for the tuberculous. Evaluation of these operations depends on a careful follow-up over a period of years to determine the number of relapses and to recognize complications which may develop. Preservation of adequate pulmonary function is essential. We have undertaken to investigate changes which may take place in the pulmonary function following resectional surgery. The present report is concerned with the changes in vital capacity and maximum breathing capacity following various types of pulmonary resection and decortication in 450 tuberculous patients. Studies on small groups of patients have shown that ventilatory function may be decreased[11] and intrapulmonary mixing altered following resection.[20, 21] Long-term studies are necessary to determine whether or not the overexpanded remaining lung loses significant function. Repeated cardiac catheterizations, over a period of years, are required to learn about the possible changes in hemodynamics resulting from pneumonectomy.

MATERIAL AND METHODS

The 450 tuberculous patients who underwent thoracic operations were mostly males. The average age was 37.5 years, range 20 to 69 years. All patients were ambulatory and in good physical condition at the time of the tests. Postoperatively, they received breathing and shoulder exercises. In addition, 40 tuberculous patients who refused surgery or were rejected by the Surgical Therapy Board were studied at similar periods to determine the effect of rehabilitation on pulmonary function. In this control group, 8 patients had minimal disease, 14 moderately advanced, and 18 far-advanced disease.

From the Veterans Administration Hospital, Madison, Wis., and the Department of Medicine and Surgery of the University of Wisconsin Medical School, Madison, Wis.

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All patients received pulmonary function screening tests 1 to 2 weeks before resection These consisted of the vital capacity performed on a 13 5 L respirometer[1] Timed vital capacity was determined by a method previously described[2] Maximum breathing capacity was done on a 13 5 L respirometer and the spirogram was used to note whether or not air trapping occurred[1] Intrapulmonary mixing of gases was analyzed by our modification[3] of the single breath test of Comroe[4] When indicated, the more complex determinations were made such as functional residual capacity residual volume, index of intrapulmonary mixing,[6] diffusion for carbon monoxide by the single breathholding techniques[7, 8] bronchospirometry, pulmonary artery pressure by cardiac catheterization, and blood gas analyses Included in this study are all patients who underwent thoracic surgery who were available in the postoperative period for re evaluation Maximum improvement in vital capacity may be anticipated within 4

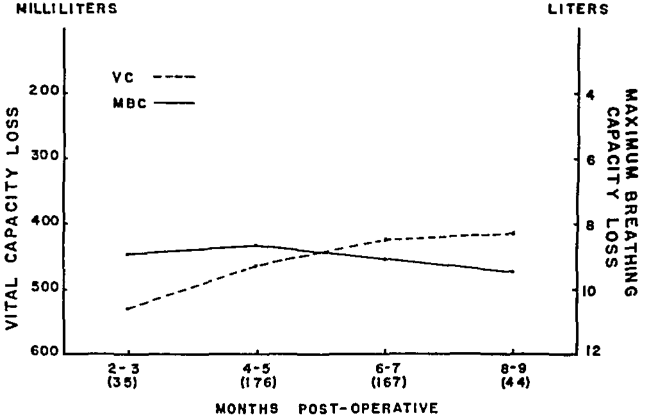

Fig 1 —Graph showing plateau in the improvement of vital capacity and maximum breathing capacity following pulmonary resection and decortication after the fifth month Numerals along the abscissa indicate the months postoperatively when tests were performed those numerals in brackets indicate the number of patients tested in each group of 2 months

to 6 months following resection as was shown by Pecora[9] in a small group of patients followed up to 6 months by serial determinations A few patients, especially following decortication, may improve their function over a period of a year or more[10] Our patients, as a group, were not tested month by month, but information on the time of maximum improvement in function may be estimated by scattergrams plotting on the abscissa the number of months after operation when the tests were completed and on the ordinate values for vital capacity and maximum breathing capacity Such scattergrams for our first 50 cases showed that a plateau of improvement was reached at the sixth month When the average changes in vital capacity and maximum breathing capacity were calculated in periods of 60 days each for the entire group, little change in function took place after the fifth month (Fig 1)

The recommendation for resection was made by a Surgical Therapy Board. The patient's problems were reviewed in detail, together with inspection of representative x-ray studies throughout the course of his disease. Planigrams and bronchograms were helpful in many patients. All patients were given long-term antimicrobial therapy. Except in the cavitary type of resection, maximum clearing and stability, according to x-ray studies, were attained before resection was considered. The majority of patients received resection to remove residual disease, but some had removal of persistent cavities. A few patients who underwent lobectomy received small thoracoplasties or insertion of an Ivalon sponge to fill the space when the remaining lung appeared incapable of expanding. Most of the patients who had pneumonectomies received large thoracoplasties or the hemithorax was filled by an Ivalon sponge.

RESULTS

Table I gives the average data for the control group. The average gain in weight between the time of the 2 tests was 4.5 pounds, 11 patients lost a few pounds, and 4 showed no change. The average time between the 2 tests was 9 months. The observed vital capacity, at the time of contemplated surgery, was 4 per cent less than the predicted value determined by the regression formula of Baldwin.[1] The follow-up study showed an increase in vital capacity over the observed value of 1.1 per cent (S.D. ± 312 ml.). The maximum breathing capacity in the control group was 14 per cent less than the predicted value[1] and the gain between the 2 tests was 5.6 per cent (S.D. ± 17 L). The studies on the control group indicate no significant gain in ventilatory function during rehabilitation. Furthermore, the data demonstrate good reproducibility of the test results after a period of months.

Table I. Averages Values for 40 Nonresected Tuberculous Patients Tested for Vital Capacity and Maximum Breathing Capacity on Two Occasions, at Time of Proposed Thoracic Operation and During Rehabilitation

	Age	40 years
	Interval between tests	9 months
	Weight gain	4.5 pounds
Vital Capacity		
First observation	Predicted vital capacity	4,032 ml.
	Observed vital capacity	3,864 ml.
	Average loss of vital capacity	168 ml.
	Per cent loss of vital capacity	4%
Second observation	Observed vital capacity	3,906 ml.
	Average gain since first test	42 ml. (S.D. ± 312 ml.)
	Per cent gain since first test	1.1%
Maximum Breathing Capacity		
First observation	Predicted maximum breathing capacity	118 L.
	Observed maximum breathing capacity	102 L.
	Average loss of maximum breathing capacity	16 L.
	Per cent loss of maximum breathing capacity	14%
Second observation	Observed maximum breathing capacity	107 L.
	Average gain since first test	5 L. (S.D. ± 17 L.)
	Per cent gain since first test	5.6%

Table II gives the pulmonary function data on the 450 patients who underwent thoracic surgery. The average interval between the preoperative value and the postoperative value was 6 months for the entire group. The average preoperative values for vital capacity and maximum breathing capacity show a decrease in pulmonary function related to the amount of diseased lung tissue as shown on x-ray examination. As might be expected the patients with pneumonectomy, many of whom had a destroyed lung, had the greatest loss before operation. Ventilatory function lost as a result of resection correlates well with the extent of lung tissue removed. Resection of a single segment caused no significant loss whereas the patients with bilateral lobectomy and pneumonectomy suffered the greatest loss in vital capacity and maximum breathing capacity. Patients who had thoracotomy for decortication but no resection of lung tissue, in contrast, had a slight gain in function.

COMMENTS

The results of these studies correspond well with those previously reported.[9-18] In general, segmental resection for localized disease causes little loss of function. Even lobectomy does not cause sufficient loss to be significant in most patients. Bilateral resection usually is done for more extensive involvement and hence there is a larger original loss as well as postoperative decrease in function. Pneumonectomy may cause a large loss of vital capacity and maximum breathing capacity except in the case of removal of destroyed lung.

In our series of 43 pneumonectomies, 29 patients had resection for scattered disease throughout one lung as demonstrated by roentgen examination and, in the majority, bronchospirometry confirmed the presence of significant functioning lung tissue. In this group the average loss of vital capacity was 37.5 per cent and loss of maximum breathing capacity 28.6 per cent. Fourteen patients had grossly destroyed lungs with a postpneumonectomy loss of vital capacity of 14.8 per cent and maximum breathing capacity of 11 per cent. Occasional large losses of function in patients having segmental resections and lobectomy resulted from complications such as hemothorax requiring drainage or re-opening the chest, extensive adhesions of the diaphragm, or inadvertent paralysis of the diaphragm.

Several articles have appeared in which the loss of function was appraised in relation to the number of segments removed for tuberculosis.[9, 16, 17, 18] The numbers reported are small and seem to include lobectomies and even pneumonectomies. The results reported therefore have questionable significance so far as segmental operations are concerned. Several investigators report good correlation of vital capacity with number of segments removed, but failed to find a positive correlation with maximum breathing capacity[16, 18] An evaluation of segmental operations according to the number of segments resected was therefore undertaken. We reviewed our material of 242 segmental resections (Fig. 2). This series includes 189 unilateral segmental resections and 53 bilateral segmental operations. Many of the patients had adjacent subsegments removed at the time of operation and some had considerable residual disease remaining

TABLE II

TYPE OF OPERATION	NUMBER OF PATIENTS	INTERVAL BETWEEN PRE-AND POSTOPERATIVE TESTS (MONTHS)	VITAL CAPACITY			MAXIMUM BREATHING CAPACITY		
			PREOPERATIVE AVERAGE (ML.)	POSTOPERATIVE AVERAGE CHANGE (ML.)	% CHANGE	PREOPERATIVE AVERAGE (LITERS)	POSTOPERATIVE AVERAGE CHANGE (LITERS)	% CHANGE
Segmental 1—3	189	6	4,460	−280	−6.3	130	−1.8	−1.4
Lobectomy	123	6.2	3,964	−413	−10.4	112	−11.2	−10.0
Bilateral *segmental*	53	5.6	4,425	−611	−13.8	132.8	−19.3	−14.4
Bilateral lobectomy and segmental	27	6.2	3,967	−688	−17.3	109	−19.0	−17.9
Bilateral lobectomies	7	5.3	3,749	−1040	−27.8	92	−25	−27.6
Pneumonectomies	43	5.7	2,968	−931	−31.4	86	−20.5	−23.8
Decortication	8	4.9	3,180	+216	+6.8	110	+12	+11.3

after cavitary resection. When segments and segments plus subsegments were tabulated, the trend remained the same, namely the more tissue removed the greater the loss of function.

A number of investigators have reported a "thoracotomy effect" which may be defined as permanent loss of pulmonary ventilatory function as a result of opening the chest without removal of significant functioning lung.[9, 16, 18, 19]

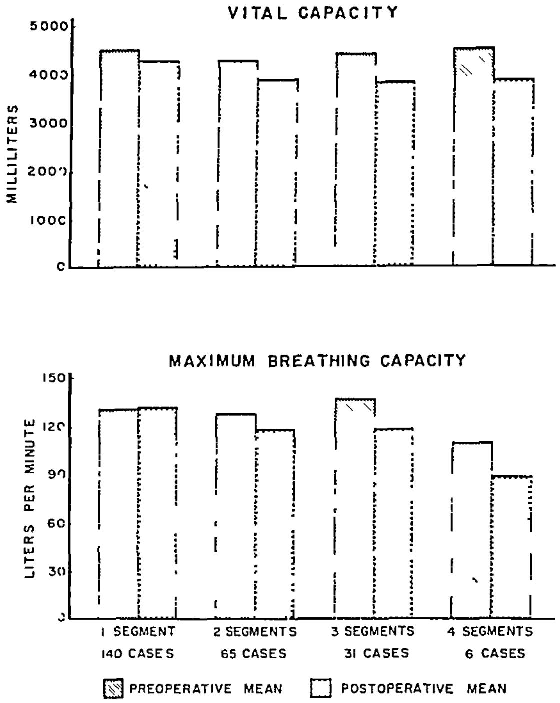

Fig. 2.—Bar graphs showing correlation between number of pulmonary segments removed and loss of vital capacity and maximum breathing capacity.

This concept seems somewhat unphysiologic. There should be no theoretical loss resulting from opening the pleura, provided no ribs are removed and no complications ensue. The application of this theory in resection of pulmonary tuberculosis is difficult to appraise because most patients lose function. However, in the large group of segmental resections the mean loss of function is very slight (vital capacity—6.3 per cent, maximum breathing capacity—1.4 per cent). There are a number of patients, particularly in the segmental group, whose function was improved. Table III lists our patients in whom improvement occurred after pulmonary resection. If "thoracotomy effect" was indeed present in these cases it is lost in the improvement noted. We suggest that "thoracotomy effect" be subjected to more critical tests before the concept is accepted.

TABLE III. PULMONARY FUNCTION DATA ON PATIENTS WHO GAINED FUNCTION DURING THE POSTOPERATIVE PERIOD

TYPE OF OPERATION	VITAL CAPACITY		MAXIMUM BREATHING CAPACITY	
	NUMBER OF PATIENTS	AVERAGE GAIN (ML.)	NUMBER OF PATIENTS	AVERAGE GAIN (LITERS)
Segmental	47	250	82	16.3
Lobectomy	26	109	35	8.6
Bilateral segmental	4	226	7	6.7
Bilateral lobectomy and segmental	2	197	2	15.5
Bilateral lobectomy			2	6.5
Pneumonectomy	2	82	5	12

SUMMARY

Four hundred and fifty tuberculous patients received preoperative and postoperative pulmonary function tests. The average interval between tests was 6 months. Excellent correlation between the extent of disease and the loss in vital capacity and maximum breathing capacity is demonstrated. Likewise, the amount of lung tissue removed and the loss of ventilatory function correlate well. When the data for segmental resections are subjected to analysis the vital capacity and maximum breathing capacity lost vary directly with the number of segments removed. The mean decrease in vital capacity and maximum breathing capacity is so slight in the segmental group of 189 patients that doubt is cast on the validity of the concept of significant loss of pulmonary function due to "thoracotomy effect."

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THE EFFECT OF BILATERAL PULMONARY RESECTION ON TOTAL OXYGEN UPTAKE AND TOTAL PULMONARY HEMODYNAMICS IN THE DOG

Michael T. Lategola, Ph.D., Walter Massion, M.D., and John A. Schilling, M.D., Oklahoma City, Okla.

AN EARLIER study[1] has defined the effects of sudden pulmonary arterial blockage (10 to 85 per cent) on pulmonary hemodynamics and gas exchange. The results of this work may be used as a basis for comparison to dogs with varying degrees of pulmonary resection.

Earlier observations[2] demonstrated that dogs manifested a good altitude tolerance and work capacity following a two-stage, bilateral removal of 56.5 per cent of their original whole lung weight. Further removal of lung tissue caused serious pulmonary crippling. It was also noted that the dogs manifested elevated right ventricular and pulmonary arterial pressures (PAP) and decreased static compliance. Postmorten examination indicated right ventricular hypertrophy and pulmonary fibrosis. These general observations suggested that a more complete evaluation of adaptive mechanisms was necessary to understand the effects of pulmonary resection and its clinical limits. This report is the first of a series to be presented on these adaptive mechanisms.

MATERIALS AND METHODS

Two-Stage Resection Sequence Employed.—The symbols and nomenclature used throughout this report to designate lung lobes are those of Rahn and his co-workers.[3] The first-stage resection consisted of the surgical removal of the medial, diaphragmatic, and mediastinal lobes (lobes BCM) of the right lung. Based on the per cent relative lobar weights of Rahn and associates,[3] these lobes constituted 70.6 per cent of the original right lung weight, and 41.1 per cent of the original total lung weight.

The second-stage resection consisted of the surgical removal of the apical and the medial lobes (lobes DE) of the left lung. These lobes constituted 36.9 per cent of the original left lung weight, and 15.4 per cent of the original total lung weight. The total quantity of lung tissue resected in both stages was 56.5 per cent of the original total lung weight.

From the Departments of Physiology, Anesthesia, and Surgery of the University of Oklahoma Medical Center, Oklahoma City, Okla.

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Time Sequence and Methods.—Eight dogs weighing approximately 20 Kg were anesthetized with Nembutal (30 mg/Kg body weight), placed in a supine position and tracheally intubated with a large bore, single lumen, cuffed polyethylene tube. For the measurements of pulmonary artery pressure (PAP), a "self guiding," flexible catheter was placed in the main pulmonary artery (PA), utilizing a technique described elsewhere.[4] The PAP was measured while the dog was breathing room air only.

The first stage resection was performed approximately 10 days following suitable preoperative control measurements of total oxygen uptake ($V_{O_2 T}$) and PAP. Postoperative measurements of $V_{O_2 T}$ were made on the tenth, twentieth, and thirty fifth days and the PAP was measured on the thirty fifth day only. The second stage resection was performed on the fortieth day following the first resection. Following the second resection, measurements of $V_{O_2 T}$ were obtained on the tenth, fortieth and eigthtieth days and the PAP was again measured on the eightieth day only.

RESULTS AND DISCUSSION

Table I summarizes the data obtained for both of the postresection periods. The $V_{O_2 T}$ was not significantly altered following both resections. The PAP measurements however indicated significant elevations following both resections. The PAP was elevated 18.2 per cent following the first stage removal of 41.1 per cent of the whole lung. The second stage removal of 15.4 per cent more of the whole lung caused a further elevation of 90.2 per cent.

It has been reported[1] that, in acute blockage of 60 per cent of the pulmonary vascular bed in supine anesthetized dogs the $V_{O_2 T}$, arteriovenous oxygen difference ($[A-V]O_2$) and cardiac output or total pulmonary blood flow (QT) manifested only slight, insignificant changes. Further, if the $(A-V)O_2$ remains unchanged in any pulmonary arterial occlusion up to 60 per cent, the change in blood flow may be calculated from the change in V_{O_2} alone. The animals were breathing 100 per cent oxygen during the whole occlusion experiment.

In a pulmonary resection of 60 per cent or less, it may be assumed that the $(A-V)O_2$ remains unchanged when the V_{O_2} is measured during 100 per cent oxygen breathing. As in the occlusion study, the change in blood flow should be proportional to the change in V_{O_2}. The total amount of lung tissue resected was 56.5 per cent of the whole lung. If the assumption of $(A-V)O_2$ constancy is utilized, then the changes in $V_{O_2 T}$, as shown in Table I, also reflect the changes in QT. The observed QT is only slightly and insignificantly altered by 56.5 per cent resection of the whole lung. Bilateral changes in Q occur, but these changes are not assessable with the data presented here. Studies to evaluate bilateral Q changes are currently under way. Since the total oxygen uptakes measured in these experiments were obtained

TABLE I

		PER CENT OF CONTROL VALUE		
	PREOP. CONTROL	10TH DAY P.O.	20TH DAY P.O.	35TH DAY P.O.
		First Resection		
$\dot{V}_{O_2}$-T	108 ± 10 ml./min. STPD	107.9 ± 5.4 P = 20.5% N = 8	104.0 ± 5.7 P = 51.5% N = 8	109.5 ± 4.5 P = 7.9% N = 8
PAP	15.5 ± 0.7 cm. H_2O			118.2 ± 5.9 P = 2.7% N = 6
R-T	100% of control			126.3 ± 9.0 P = 1.5% N = 6
		10TH DAY P.O.	40TH DAY P.O.	80TH DAY P.O.
		Second Resection		
$\dot{V}_{O_2}$-T	108 ± 10 ml./min. STPD	100.9 ± 2.8 P = 76.5% N = 5	98.8 ± 3.6 P = 76.3% N = 4	99.4 ± 5.4 P = 91.9% N = 4
PAP	15.5 ± 0.7 cm. H_2O			208.4 ± 13.2 P = 0.9% N = 3
R-T	100% of control			271.6 ± 8.6 P = 0.4% N = 3

Legend: P.O. = postoperative; P = probability value (<5.0% indicates statistical significance); N = number of data.

under anesthesia, they represent estimates of resting stage values. A priori, one should expect decreases in the maximal $\dot{V}_{O_2}$-T and $\dot{Q}$-T. These two parameters afford a measure of the changes in reserve capacity available to the animal in the postresection state. The maximal $\dot{V}_{O_2}$-T and/or $\dot{Q}$-T immediately following the resections should drop proportionally to the amount of lung removed. Any adaptive increase in these two parameters, consequent to the resections, must be due to vasodilatation and/or recapillarization of the remaining lung tissue. There is some evidence to support the idea that the latter type of compensation may occur.

Although there were only slight, insignificant changes in $\dot{Q}$-T following both resection stages, the concomitant PAP elevations indicate that changes in total vascular resistance (R-T) have occurred. The R-T of the pulmonary vascular bed may be calculated from the following mathematical expression:

$$\text{R-T} = \frac{\Delta P}{\dot{Q}\text{-T}} = \frac{\text{PAP-PVP}}{\dot{Q}\text{-T}}$$

Where: ΔP = "the pressure head" of the system,
and PVP = mean pulmonary venous pressure.

In the above expression, if it is assumed that $\dot{Q}$-T remains unchanged following resection, then the change in R-T becomes proportional to the change in ΔP. Borst and his associates[5] have reported that, in anesthetized, thoracotomized dogs, whole $\dot{Q}$-T was held constant by a perfusion pump, a serotonin injection into the right PA produced a fall in $\dot{Q}$-RT, a rise in $\dot{Q}$-LT and a large rise in PAP but only a small, insignificant rise in PVP Stroud and Rahn[6] have reported that hypoxically induced PAP increases in the dog were accompanied by only slight, insignificant changes in PVP and Q T The maximum average increase in PAP due to 8 per cent inspired oxygen (as compared to room air) was from 17 5 to 26 3 cm H_2O or equivalently, 150 per cent of the control values The average PVP before and during 8 per cent oxygen breathing was approximately 4 5 cm H_2O In these resection experiments, if it is assumed that Q-T and PVP remain unchanged and that the PVP has a value of 4 5 cm H_2O, then it is possible to calculate the average changes in R T following both resections These calculated data are found in Table I Both increases are significant at the 5 0 per cent level of probability These results parallel the previously mentioned PAP data, that is, whereas the R T increased 26 3 per cent as a result of the removal of 41 1 per cent of the whole lung, the removal of only 15 9 per cent more of the whole lung caused a further disproportionate increase of 145 3 per cent

The pressure/flow curve reported by Lategola[1] for passively induced, increased pulmonary Q in the supine, anesthetized dog indicates that an acute pulmonary arterial occlusion, equivalent to the removal of 41 1 per cent of the whole lung, produces a PAP increase of approximately 33 per cent Since the PAP, 35 days following the first resection, was elevated only 18 2 per cent, some hemodynamic adaptation occurred It was hypothesized that the PAP difference between the acute blockage and resection of 41 1 per cent of the whole lung indicated a substantial degree of new recapillarization or capillary opening in the right apical lobe From other gross observations[7] of substantial weight and size increases in this lobe, we feel that its vascular resistance was initially increased due to capillary stretching accompanying its size increase and that consequent to this occurrence, new capillaries were adaptively formed or opened

Following the second resection The PAP and R T increases are greater than those of both the theoretical predictions and the acute pulmonary arterial blockage of the same degree This analysis, coupled with the gross observations of minimal weight and size increases[7] of the left lower lobe following the second resection, suggests that little adaptive change takes place in this lobe Since this does not seem to occur in the left lower lobe, lobar adaptation to resection may not only depend on the degree of resection and remaining lobar masses involved, but also on the initial position of the particular lobe in the thorax An investigation of this phenomenon is currently in progress

SUMMARY

The $V_{O_2\,T}$ and Q T are only slightly and insignificantly altered following 56 5 per cent bilateral resection of the whole lung The PAP and R T are increased following both resections but disproportionally increased following the second resection

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SCALENE NODE, PARIETAL PLEURA, AND LUNG BIOPSY IN THE DIAGNOSIS OF INTRATHORACIC DISEASE

John W. Smith, M.D., Harry G. Parsons, M.D.,** and*
*Albert C. Daniels, M.D.,*** Weimar, Calif.*

THE MORBIDITY of exploratory thoracotomy in the diagnosis of pulmonary disease may often be avoided by the judicious use of scalene node biopsy, pleural biopsy, and/or lung biopsy.

SCALENE NODE BIOPSY

Since the technique was first described by Daniels[10] in 1949, there have been many reports confirming its usefulness.[1, 2, 4, 6, 8, 9, 12, 17, 19, 21, 28, 30, 33, 37, 41, 43, 44] Pathologic diagnoses have been made in sarcoidosis, carcinoma of the lung, tuberculosis, lymphomas, metastatic carcinoma, silicosis and histoplasmosis. Harken and his associates[17] demonstrated that the incidence of positive findings, especially in carcinoma of the lung, was greatly increased when the dissection was carried as far into the mediastinum as possible. He stressed Rouvière's[29] concept of the lymphatic drainage of the lung. The lymphatic drainage of the lower part of the left and the entire right lung is to the right scalene lymph nodes. Left upper lobe lesions drain to the left scalene area, mid lung or hilar lesions on the left may drain to either side. The frequency of positive node biopsy has varied from 6[19] to 66 per cent.[4] Of a total of 1,311 cases,[4, 6, 9, 12, 17, 19, 21, 28, 30, 33, 37, 41, 43, 44] a positive diagnosis was obtained in 391, or 34 per cent. In these reports, the best yield has usually been in cases of sarcoidosis and in the various lymphomas. However, the technique has been used extensively to determine operability in malignancies of the lung and mediastinum. An excellent review of the anatomy of the prescalene region[16] appeared in 1956.

Technique. Scalene Node Biopsy.—Selection of side for biopsy is done following the concepts of the lymphatic drainage of the lung.[9] The right side is chosen for lesions of the right lung and the left lower lobe. The left side is biopsied for lesions of the left upper lobe. The patient receives preoperative medication as for any procedure under local anesthesia.

From Weimar Chest Center, Weimar, Calif.
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*Assistant Resident in Surgery, Stanford University Hospitals.

**Chief of Surgery, Weimar Chest Center, and Clinical Instructor in Surgery, Stanford University School of Medicine.

***Consultant in Surgery, Weimar Chest Center, and Asst. Clinical Professor of Surgery, Stanford University School of Medicine.

A pillow is placed beneath the shoulders (elevating the shoulder on the side to be operated) and the head is turned away from that side. A local anesthetic is infiltrated into the line of proposed incision and the tissues beneath. A 5 to 7 cm. incision is made parallel to the upper border of the clavicle and about 2 cm. above it, being centered over the lateral border of the sternocleidomastoid. The platysma is divided in the same line and reflected off the superficial layer of the deep cervical fascia for a short distance upward and downward (Fig. 1). The lateral border of the sternocleidomastoid is then mobilized and retracted medially, which brings the internal jugular vein into view. The posterior belly of the omohyoid is mobilized from the underlying fat pad, and the fat pad with its contained lymph nodes is dissected from the scalene muscle (Fig. 2, *A*), carefully preserving the phrenic nerve in the fascia of the muscle (Fig. 2, *B*). The transverse cervical artery and vein pass through this fat pad and may be divided and ligated if necessary. The lower limit of the dissection is behind the subclavian vessels, being careful to preserve the thoracic duct (on the left side) or the right lymphatic duct. A finger may then be used to explore the upper part of the mediastinum along the great vessels. The wound is closed in layers.

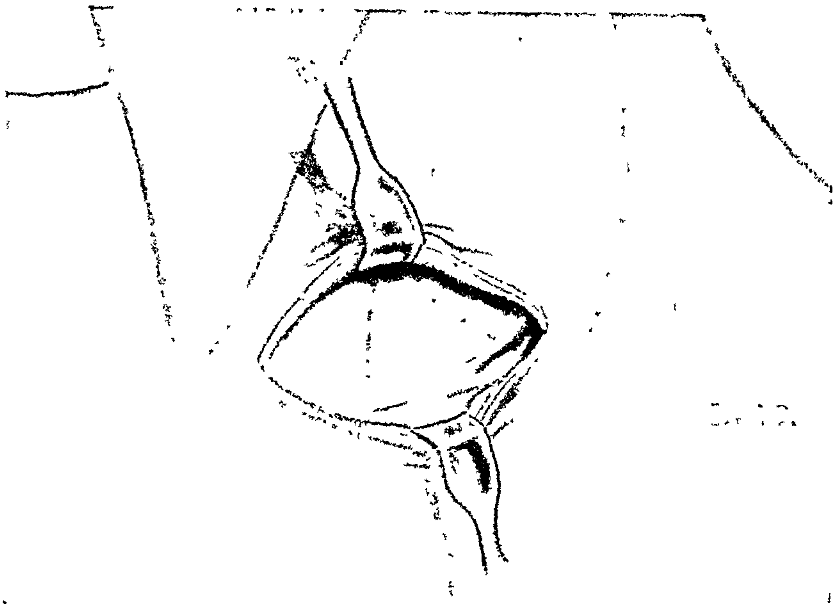

Fig. 1.—Scalene Node Biopsy. Incision through skin and platysma has been made revealing the superficial layer of the deep cervical fascia with the underlying scalene fat pad in the area bounded by clavicle, omohyoid, and sternomastoid.

It is important to dissect carefully the specimen in a sterile manner. All lymph nodes found should be divided in half; one part to be sent to the pathologist, the other to the bacteriology laboratory for culture. We have had the nodes cultured routinely for *Mycobacterium tuberculosis.* Fungal cultures are ordered when desired.

Scalene node biopsy has been performed on 50 Weimar Chest Center patients since January, 1950, 2 having bilateral biopsies. Their ages ranged from 7 to 84 years. There were 19 positive diagnoses obtained, or 38 per cent.

Most common diagnoses (Table I) were metastatic carcinoma of the lung, tuberculosis, sarcoidosis, and metastatic tumor from sites other than the lung. Of the 9 cases of proved carcinoma of the lung, 2 had been diagnosed by bronchoscopic biopsy, and the scalene nodes were taken for evidence of operability. Four cases were proved by the scalene node examination alone. The 4 patients with negative scalene nodes were subjected to thoracotomy, only one was operable.

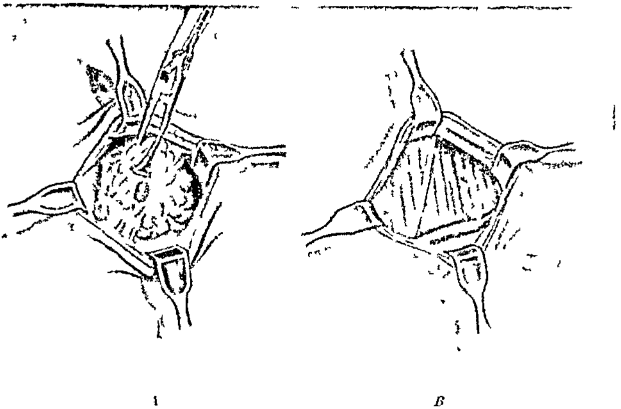

Fig. 2.—Scalene Node Biopsy. *A*, The fat pad with its contained lymph nodes has been freed from the jugular vein.

B, With the fat pad removed the jugular and subclavian veins, the clavicle, and the anterior scalene muscle with the accompanying phrenic nerve, are seen. The transverse cervical artery and vein and the thoracic duct are not shown.

TABLE I. SCALENE NODE BIOPSY

DIAGNOSES	TOTAL CASES	NUMBER POSITIVE	PER CENT POSITIVE
Carcinoma of lung			
Proved cases	9	5	56
Suspected cases	4	0	0
Tuberculosis	13	4	31
Tuberculosis and silicosis	1	1	
Silicosis	2	0	0
Sarcoidosis	2	2	
Lymphoma	2	2	
Metastatic carcinoma, primary unknown	3	3	
Other	14	2	14
Totals	50	19	38
Other			
Carcinoma of esophagus	2	1	
Carcinoma of rectum	1	1	
Multifocal interstitial fibrosis of lung	1	0	
Idiopathic pulmonary hemosiderosis	1	0	
Multiple pulmonary abscess	1	0	
Histiocytosis	1	0	
Bronchiectasis	1	0	
Heart failure with pulmonary congestion	1	0	
Undiagnosed pulmonary disease	5	0	

PLEURAL BIOPSY

Three methods of pleural biopsy have been discussed in the medical literature: biopsy with thoracoscopy,[24] needle biopsy, using a Silverman needle,[3, 11, 13, 18] and biopsy with direct visualization, whether by a small incision,[2, 3, 34, 35] or at open thoracotomy.[34, 35] The method involving thoracoscopy never proved popular. Those who have done both needle and open biopsies[3] have abandoned use of the needle because they feel the specimen obtained at open biopsy is so far superior and the technique no more difficult. The authors who advocate needle biopsy report adequate tissue for diagnosis in 45 per cent[18] and 73 per cent.[13] The latter group did open biopsy where possible when inadequate tissue was obtained or when they got a report of "non-specific pleuritis." These additional biopsies were productive of 5 cases of granulomatous pleuritis and 2 of malignancy in the group of 10 cases. Contrasted with this uncertain situation is the fact that the tissue obtained at open biopsy can be selected under direct vision from an obviously diseased area. There is no reason for inadequate material.

Technique: Pleural Biopsy.—The area for biopsy is determined by examination of the chest roentgenogram. The patient is positioned to make this area accessible. He is given preoperative sedation and, when he enters the operating room, he is made familiar with the anesthetist's mask and the sensation of breathing against positive pressure. Intercostal nerve blocks are placed to anesthetize the area selected. A local anesthetic agent is infiltrated into the skin and subcutaneous tissues in the line of proposed incision. The incision, usually 7 to 10 cm. long, is carried down to the rib. The periosteum is then reflected, the rib elevated, and the pleura beneath it exposed. An area of pleura is then easily removed (Fig. 3). If a free pleural space is present, this will cause immediate pneumothorax which can be controlled by positive pressure breathing. If the biopsy is done in the lower part of the chest, the diaphragmatic pleura can often be biopsied also. One should be careful to select a representative area, such as any thickened or obviously abnormal section of the parietal pleura. A large rubber catheter is brought out through a stab wound in an adjacent interspace and connected to water-seal drainage. The wound is closed in layers. A small part of each area of pleura is sent for culture for *M. tuberculosis.* The remainder of the specimen is sent to the pathologist. The catheter is removed after 24 hours, unless there is some indication for continued drainage.

Twenty-five cases of pleural biopsy have been done at Weimar Chest Center since 1950. In only one had *M. tuberculosis* been isolated from the pleural fluid: the biopsy was done after a year of therapy in this patient. In all remaining cases, acid-fast bacilli had not been found in pleural fluid, sputum, or gastric contents previous to biopsy. Many of these patients had no fluid present at the time they reached our hospital. In 5 of the cases tuberculosis was later demonstrated by sputum cultures. Of the 25 patients, 17 had a histologic diagnosis of tuberculous pleuritis, and in 10 of these, acid-fast bacilli grew on culture of the pleural tissue. Two more patients were found to have chronic pleuritis suspicious of tuberculosis with negative cultures Nontuberculous pleuritis and normal pleura were found in 5 cases, and a large cell carcinoma metastatic to pleura in one. One of the patients diagnosed as having subacute pleuritis continued to form pleural fluid, and a later thoracentesis was productive of acid-fast bacilli on culture This was the only false negative in our series. The remaining 5 patients were spared the long period of hospitalization and treatment which would be necessary for a diagnosis of "idiopathic pleural effusion, presumably tuberculosis"

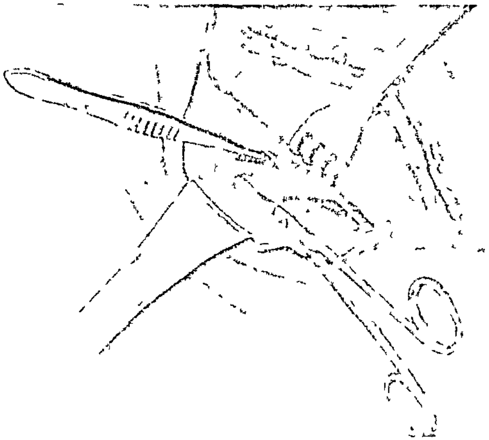

Fig 3—Biopsy of Parietal Pleura With the rib bed exposed, a segment of the parietal pleura is excised

Table II. Pleural Biopsy

DIAGNOSIS	CASES	PER CENT
Tuberculous pleuritis	17	68
Chronic pleuritis suspicious of tuberculosis	2	8
Subacute or chronic pleuritis (nontuberculous)	4	16
Large cell carcinoma, metastatic to pleura	1	4
Normal pleura	1	4
Total	25	

LUNG BIOPSY

Biopsy of pulmonary tissue has been an accepted procedure for some time when considered in the sense of exploratory thoracotomy with biopsy, especially for isolated pulmonary nodules. The more diffuse pulmonary lesions have not received this kind of attention until recently In 1949, Klassen, Anlyan, and Curtis[23] reported on a new technique of limited thoracotomy through a short intercostal incision with biopsy of the peripheral lung which presented itself They reported 6 cases including sarcoidosis, tuberculosis, and metastatic malignancy. Since that time, pulmonary beryllosis, silicosis, asbestosis, anthracosis, interstitial fibrosing pneumonitis, pulmonary fibrosis, emphysema, atelectasis, chronic pneumonitis, and chronic passive congestion have also been found on examination of material taken by limited lung biopsy.[1, 2, 5, 8, 15, 26, 39, 10] Hamman-Rich syndrome, pulmonary telangiectasia, and eosinophilic granuloma, as well as some of the conditions listed above, have been reported as diagnosed by biopsy at standard, open thoracotomy.[7, 22, 27, 37, 42] Perhaps some saving in patient comfort could have been made if in these cases there had been only the limited form of biopsy. Needle biopsy of the lung[8, 14, 25, 30] is best reserved for patients who have incurable peripheral pulmonary malignancy in whom a tissue diagnosis is desired before starting palliative treatment.

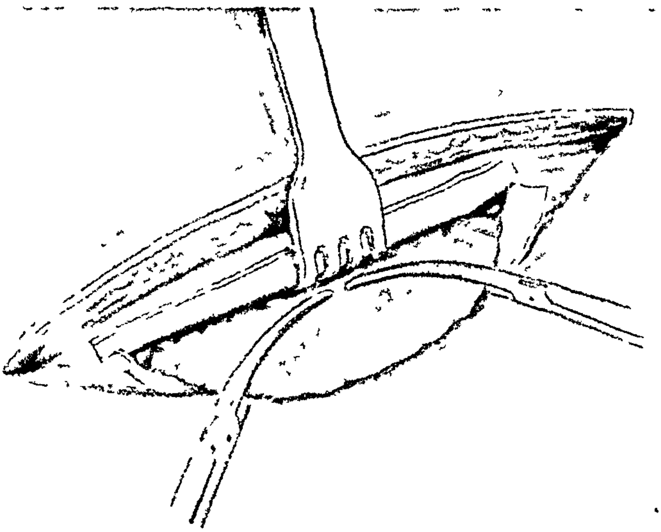

Fig. 4.—Biopsy of Lung The pleura has been opened and one margin of an adjacent lobe containing palpable disease is selected for a wedge resection

Technique: Lung Biopsy.—Site of biopsy is again based on the chest roentgenogram. In most cases of diffuse pulmonary infiltration, a biopsy from the margin of the middle lobe or lingula would include representative tissue; therefore, the most common site of biopsy is the fifth rib anteriorly, on either side. The patient is sedated and placed to make the operative site accessible. The anesthetist helps the patient become accustomed to positive pressure breathing via the face mask. Intercostal blocks are placed and the skin infiltrated with anesthetic. The rib bed is exposed in exactly the same manner as in pleural biopsy, and the pleura opened. It is usually not necessary to resect any part of the rib, but this may be done if desired to facilitate exposure. A limited exploration can be carried out to select an area for biopsy. Pneumothorax is controlled by positive pressure. A representative wedge-shaped area is excised using crushing clamps (Fig. 4), and the lung is closed by a continuous mattress suture oversewn by a continuous lock stitch using absorbable suture A catheter is left in the pleural space through a stab wound and the wound closed in layers A portion of the specimen may be submitted for culture and the remainder fixed for histologic examination If proof of pneumoconiosis is desired, part of the specimen can be sent for the desired analysis The catheter is connected to water seal drainage, and may be removed in 24 hours if no air leak or bleeding is present

There have been 9 cases of lung biopsy (in the limited sense used here) at Weimar Chest Center since 1952 These were patients in whom diagnosis was not otherwise established Diseases found in this series are listed in Table III Study at autopsy on the case listed as 'atelectasis with chronic pneumonitis" later revealed a diagnosis of idiopathic pulmonary hemosiderosis Special stains had not been made on the biopsy specimen and, in retrospect, it is felt that the diagnosis could have been made from the biopsy material The case of granuloma of the lung was not cultured

TABLE III LUNG BIOPSY

DIAGNOSIS	CASES
Tuberculosis	3
Granuloma (nonspecific) of lung	1
Sarcoidosis	1
Anaplastic carcinoma, origin unknown	1
Histiocytosis	1
Atelectasis with chronic pneumonitis	1
Vesicular emphysema	1

DISCUSSION

Scalene node biopsy is most useful in cases of sarcoidosis lymphoma, and malignancy in the lung and mediastinum, whether primary or secondary It is of particular value in determination of operability in carcinoma of the lung, since evidence of metastasis to the scalene nodes makes resection for cure impossible Other diseases will also show evidence of involvement of these nodes tuberculosis, silicosis, histoplasmosis, and other malignancies As is true of other biopsy techniques a negative report does not exclude any disease We include anthracosis, hyperplasia, and lymphadenitis under the term ' negative "

Pleural biopsy is indicated when there is evidence of effusion or pleural thickening on x ray study without proved etiology This method has also been advocated to save time, in that a histologic diagnosis may be obtained in a day or two as compared with 6 weeks for culture of tuberculosis In younger age groups, the most common diagnosis will be tuberculous pleuritis, while malignancy will be more frequent in older persons

Lung biopsy is indicated in diffuse, usually bilateral, pulmonary infiltrations in which other methods have not yielded a positive diagnosis Sarcoidosis, pulmonary fibrosis, pneumoconiosis, and certain types of tuberculosis and metastatic malignancy, the diseases most commonly found by this method, are not amenable to surgical treatment and there is no need for thoracotomy of the classic type for definitive treatment of the disease. The medical management varies in each of these conditions. Hence the importance of a correct diagnosis. Unfortunately, some of the specimens will not be diagnostic of a specific disease process, but will be reported as chronic pneumonia, chronic granuloma, and pulmonary fibrosis. These entities are poorly understood. The clinician must always keep in mind the possibility of multiple disease processes. The diagnosis of tuberculosis, for example, does not exclude a carcinoma of the lung in the same patient.

The addition of these three diagnostic techniques should reduce further the number of cases bearing the word "suspected" on the final diagnosis.

SUMMARY

An accurate diagnosis can often be made in pulmonary diseases by use of one or more techniques of biopsy which may spare the patient the morbidity, time, and expense associated with thoracotomy.

These techniques, in addition to the well-known laboratory, x-ray, and endoscopic procedures, include biopsy of the scalene lymph nodes, of the parietal pleura, and of the peripheral parts of the lung tissue itself.

Fifty cases of scalene node biopsy are reported with positive results in 38 per cent on histologic study. This procedure is most useful in diagnosis of sarcoidosis, lymphoma, and metastatic malignancy. It is of particular use in determination of operability in carcinoma of the lung.

Twenty-five cases of pleural biopsy are reported, with tuberculous pleuritis as the most common finding. One study gave a false "negative" report, since the patient was later proved to have tuberculous pleural effusion. This technique is of particular value in the case of "idiopathic pleural effusion" or thickened pleura. It will often shorten the time required to make a diagnosis even though such diagnosis could be made by other, slower means.

Nine cases of lung biopsy through a limited incision are reported. This technique is of value in cases of diffuse pulmonary infiltrations in which an accurate diagnosis cannot be made by other means. These diseases are medical in nature and do not require definitive surgical treatment at the time of biopsy. Therefore, a large thoracotomy incision is not required. Another indication for lung biopsy is the suspected presence of a compensable disease.

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CERVICAL MEDIASTINOTOMY FOR BIOPSY

John D. Steele, M.D., San Fernando, Calif., and
Samuel A. Marable, M.D., Los Angeles, Calif.

In the decade since Daniels' original report,[1] diagnostic biopsy of the prescalene fat pad and its contained lymph nodes has become a widely accepted technique. The value of this procedure in providing a tissue diagnosis of both inflammatory and neoplastic disorders within the thorax has been shown many times and reported by various authors.

In instances in which suspicious nodes are palpable in the supraclavicular area, cervical lymph node biopsy gives confirmatory evidence of inflammation or neoplasm in a high percentage of cases. When, however, no nodes are palpable in this area, scalene node biopsy is understandably less satisfactory in providing positive results. Unfortunately, it is in this last group of cases that biopsy might be most valuable. Consequently, attempts have been made to increase the frequency of positive biopsy results by modification and extension of the original technique. The purpose of this report is to describe a surgical approach to the prescalene and paratracheal lymph nodes which we feel has certain advantages over those previously reported.

The generally accepted limits of dissection in scalene node biopsy include the internal jugular vein medially and the subclavian vein inferiorly. In 1954, Harken and his associates[2] proposed extension of the dissection into the upper mediastinum through the classic incision, utilizing a laryngoscope when necessary to provide exposure of the paratracheal tissues in this area. In this manner, biopsy specimens could be obtained from the paratracheal nodes within the thorax. Their series of 142 such procedures yielded 31.7 per cent positive results in cases of pulmonary carcinoma with nonpalpable supraclavicular nodes. It was emphasized that half of the positive results were obtained from the paratracheal nodes, and would have been missed if scalene biopsy alone had been employed. Despite this improvement in results, the mediastinal extension of the operation has not gained wide acceptance. The reason for this lack of acceptance apparently stems from the inadequate exposure of the mediastinal area afforded by this approach, with its [illegible]

From the Veterans Administration Hospital, San Fernando, Calif., and from the Department of Surgery, University of California, Los Angeles, Calif.

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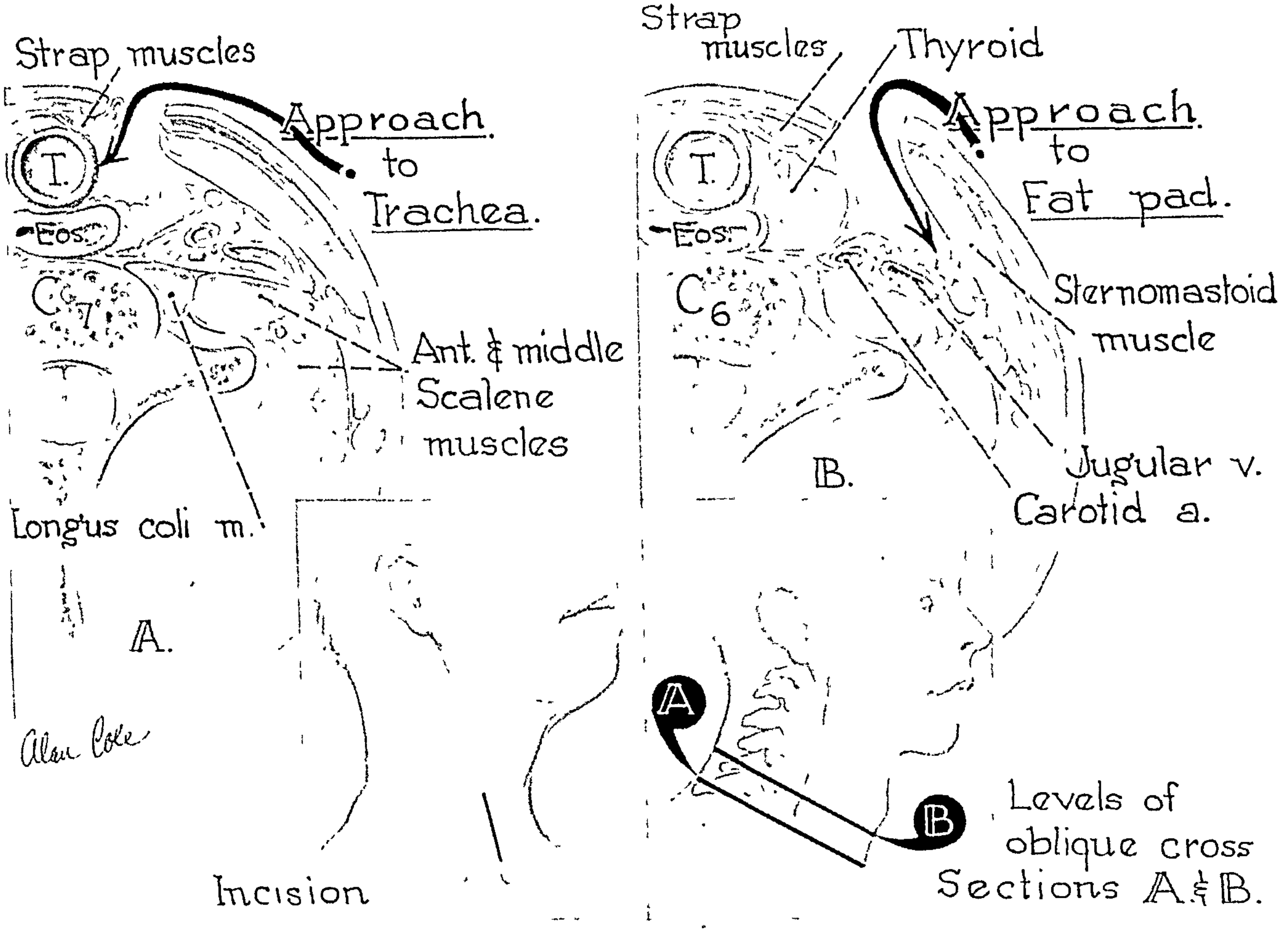

Fig. 1.—The skin incision for cervical mediastinotomy is shown in the inset on the left. The levels of the oblique cross sections, A and B, are indicated in the inset on the right. The approach to the trachea can be made by blunt dissection after the anterior border of the sternomastoid muscle is reached, as indicated by the arrow in A. Following the mediastinal dissection, the prescalene fat pad can be approached by blunt dissection posterior to the sternomastoid muscle as indicated by the arrow in B

dangers of serious hemorrhage and pleural perforation From subsequent publications, one gains the impression that the increase in positive results by mediastinal dissection has not justified the increased risk of the procedure

We have been using the technique for cervical mediastinotomy employed for many years for the exposure of the upper esophagus and for drainage of mediastinal abscesses[3] Under local anesthesia a 5 to 7 cm incision is made over the anterior border of the sternocleidomastoid muscle with its lowest point in the suprasternal notch (see inset in Fig 1) After the skin and fascia have been incised, blunt dissection can be employed almost entirely Dissection is carried inferiorly and mesially to the carotid sheath through the middle cervical fascia to the trachea (see *A* in Fig 1) The sternothyroid muscle is retracted although it could be split longitudinally if necessary One easily enters the paratracheal areolar tissue and, by gentle finger dissection, this plane is opened down to the level of the aortic arch on the left side and to a comparable distance on the right side These levels have been verified roentgenographically by placing radiopaque catheters temporarily in the depths of the wound, the tips of the catheters being visualized at the level of the second costal cartilage It is possible to examine the paratracheal area under direct vision, to palpate thoroughly, and to obtain a biopsy of any suspicious areas which may be present In addition, masses in the apex of the lung may be palpated laterally and needle biopsy may be performed under direct vision, making this a safer procedure than is possible through the chest wall

Following the paratracheal portion of the procedure, dissection may be carried laterally between the posterior surface of the sternocleidomastoid and the anterior margin of the carotid sheath to expose the scalene fat pad (see *B* in Fig 1) A completely satisfactory biopsy of the fat pad may be obtained from this approach The most lateral portion of the pad may be somewhat difficult to expose, but with adequate retraction even this portion may be excised The more medial and inferior portions of the pad perhaps the most valuable for diagnostic purposes are removed with great ease through this approach The wound is closed in layers without drainage

The group of cases in which this technique has been used is too small for statistical analysis No significant complications have been encountered and there have been no instances of damage to major vessels or nerves nor have there been any pneumothoraces The dissection must be carried out carefully, however, since in addition to the structures encountered in routine scalene biopsy, the inferior thyroid veins lie in the area of dissection These vessels may, of course, be ligated and divided if necessary The recurrent laryngeal nerve, lying in the tracheoesophageal groove, is posterior to the operative field, but its location must also be kept in mind

It is our belief that this technique results in a significant increase in positive biopsy results without a significant increase in the operative risk The results in our cases apparently confirm the advantages of paratracheal biopsy reported by Harken and his associates. Although the area of dissection is the same as they described, we feel that the approach we have employed is more versatile and has added safety in being performed entirely under direct vision.

SUMMARY

A modified approach for the combined biopsy of paratracheal and prescalene lymph nodes has been described which can be performed with relative safety under direct vision.

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PAPILLOMA OF THE ESOPHAGUS

Association With Hiatal Hernia

Richard H. Adler, M.D., David M. Carberry, M.D., and
Charles A. Ross, M.D., Buffalo, N. Y.

Benign tumors of the esophagus, although uncommon, have received increasing attention in recent years. They may be divided into two main groups, intramural and intraluminal. Intramural tumors generally produce few symptoms unless they attain a large size. They rarely protrude in a pedunculated manner into the esophageal lumen. Generally, the tumors are well circumscribed, and they may often be shelled out of the esophageal wall without opening the mucosa. A small number may undergo malignant change. Intraluminal tumors, particularly those arising mainly from the esophageal mucosa, have been considered to be rare. Our understanding of their pathogenesis is limited.

Polyps were among the first of the benign intraluminal tumors of the esophagus to be described. An intraluminal polyp may elongate from the action of peristalsis and swallowing until the pedicle assumes a length that may allow the growth to be regurgitated into the throat. Totten and his associates[14] found 40 polyps of the esophagus reported in the literature. All were in adults, and 34 originated in the upper third of the esophagus. Benign intraluminal tumors may also originate from heterotopic areas of gastric or intestinal epithelium as well as from the esophageal glands.

Perhaps the lesions causing the greatest confusion are the sessile intraluminal tumors which have been described as wart-like protuberances or small polypoid, papillary growths. To this ill-defined group the term papilloma has occasionally been attached. The distinctions between esophageal papilloma, localized mucosal hyperplasia, granulomatous proliferation, leukoplakia, epithelioma, and certain small sessile polyps become muddled due in part to the use of indiscriminate terminology and loose interpretation. Incomplete clinical documentation and meager pathologic descriptions of reported cases add to the many uncertainties.

The literature contains conflicting reports as to the nature of papilloma of the esophagus. Stout and Lattes[12] have recently stated that true papillomas of the human esophagus do not exist. Terracol and Sweet,[13] however,

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From the Roswell Park Memorial Institute and the Department of Surgery, University of Buffalo School of Medicine, Buffalo, N. Y.

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mention papillomas of the esophagus as a not uncommon finding at autopsy. Esophageal papillomas are known to occur in certain animals. When the literature on papilloma of the human esophagus is reviewed, one is impressed by the fact that practically all case reports called papilloma of the esophagus were published over 20 years ago.[2-6, 9-11] The papillomas were diagnosed on the basis of small pieces of tissue removed by esophagoscopic biopsy. Unfortunately, for the most part, the diagnosis was merely stated without any adequate pathologic description.

The few publications mentioning papilloma of the esophagus other than the earlier case reports refer back to the papers of Patterson which appeared between 1927 and 1933.[9-11] Patterson found 62 cases of benign esophageal neoplasms in the period 1717 to 1932. These included postmortem diagnoses, and many apparently had little detail other than the name of the doctor and the type of growth. In listing the types of neoplasms found in this review, Patterson stated that 8 were papillomas. Unfortunately, there was no review of the 8 papillomas and the references were not complete.

In reporting a case of papilloma of the lower esophagus in 1931, McKinney[6] mentioned that Jackson had informed him by personal communication of 3 cases of papilloma of the esophagus he had seen. Moersch and Harrington[7] in 1944 stated that 44 benign tumors of the esophagus were found in 7,459 postmortem examinations at the Mayo Clinic in patients without esophageal complaints. The list of tumors included 3 papillomas of the esophagus but no further description or comment was made concerning the papillomas. In 1945, Adams and Hoover[1] referred to Patterson's study and added 26 additional benign tumors of the esophagus found from 1933 to 1943. They also added 3 cases of their own to make a total of 91 benign tumors of the esophagus recorded in the literature. In listing all cases, they included the 8 cases of papilloma of the esophagus mentioned by Patterson and one other papilloma for the 1933 to 1943 period. This additional papilloma was only listed and no further detail was supplied. Since that time, most reports on benign tumors of the esophagus omit papillomas entirely, mention the condition in passing, or briefly refer to the cases previously reported.

Recent experience with a patient having a localized, sessile tumor in the distal esophagus, which was diagnosed histologically as papilloma, stimulated our interest in this subject and prompted a review of our own records and the available literature. This is apparently the first documented case of papilloma of the esophagus associated with hiatal hernia and distal esophageal stenosis. To our knowledge, it is also the first case in which thoracotomy was performed with resection of the tumor and the involved esophagus.

On reviewing our clinical material for the 11-year period, January, 1947, to December, 1957, 205 cases of carcinoma of the esophagus were found. In 4, there were esophagoscopic biopsies proximal to an esophageal malignancy that were reported as papilloma of the esophagus, but this diagnosis was not upheld when the material was re-examined at the time of this review. Certain aspects of papilloma of the esophagus will be reviewed in this paper based upon our clinical experience and the information gathered from the literature.

CLINICAL MATERIAL

A Papilloma of the Esophagus Associated With Hiatal Hernia and Stricture (Case Report).—

J. M. (No. 92972), a 73-year-old white man was admitted to the Roswell Park Memorial Institute on March 6, 1958, with the chief complaint of intermittent but progressive dysphagia for 2 years. This was characterized by a sensation of food sticking in the lower chest. He denied heartburn, pyrosis, regurgitation, or flatulence. There had been no weight loss.

On physical examination, the patient appeared to be in fair health. He was edentulous. Barium roentgenographic studies of the upper gastrointestinal tract showed a hiatal hernia with narrowing at the cardioesophageal junction (Fig. 1). The radiologist felt that the stenosis was secondary to a long-standing hiatal hernia and that there was no evidence of neoplasm. The narrowed area could not be distended. There had been no previous x-ray studies.

Esophagoscopy on March 7, 1958, showed the esophagus to be normal until a level 33 cm. from the upper incisor teeth was reached; here, a papillary tumor was encountered arising from the left posterolateral aspect of the esophagus. When efforts were made to pass the esophagoscope beyond the growth, the tumor protruded partially into the esophagoscope and prevented further passage. This papillary lesion projected approximately 1 cm. into the esophageal lumen and arose from an area roughly 1.5 cm. along the esophageal circumference. Its surface appeared pink with irregular small lobulations. Four biopsies were taken from the growth with only minimal bleeding. Washings were aspirated for tumor cells. The gross impression was probable carcinoma of the esophagus proximal to a hiatal hernia. There was no evidence of esophagitis, fissuring, leukoplakia or mucosal hyperplasia. The histologic report of the biopsy material was papilloma of the esophagus with no evidence of malignancy either in the specimen or esophageal washings.

On March 21, 1958, a second esophagoscopy was done with the preoperative diagnosis of probable carcinoma of the esophagus and hiatal hernia. The same findings were encountered and several large pieces of the neoplasm were removed with biopsy forceps. The sites of the previous biopsies could be seen. It was not possible to pass the esophagoscope beyond the growth. Again the impression was that of an esophageal tumor, most probably carcinoma. Histologically the biopsies were the same as those of the first examination.

After considerable discussion, it was agreed that the patient should have a thoracotomy and esophageal resection for the following reasons: (1) a somewhat chronic history of slowly progressive esophageal obstruction in an otherwise healthy individual, (2) the possibility of an associated underlying neoplasm despite the negative biopsies and long history, (3) a desire to comply with the patient's wishes for surgical relief of his troublesome dysphagia. On March 31, 1958, thoracotomy was performed through the bed of the left seventh rib. Upon opening the mediastinal pleura, the hiatal hernia with a secondarily shortened esophagus was readily apparent. The esophagus appeared to be entirely normal on inspection. Palpation revealed a localized area approximately 3 cm. proximal to the esophagogastric junction that felt soft and thickened as compared with the rest of the esophagus. According to the preoperative plan, the esophagus over this area was opened longitudinally for a distance of 5 to 6 cm. The mucosa of the esophagus appeared to be normal but a small, sessile, smoothly lobulated lesion, slightly over 1 cm. size, was visible on the left posterolateral wall of the esophagus (Fig. 2). The sites of previous esophagoscopic biopsies were seen adjacent to this growth. There was no gross evidence of esophagitis, mucosal hyperplasia with fissuring, or carcinoma. Distally a definite stenosis was noted at the esophagogastric junction that barely admitted the tip of the operator's fifth finger. After considerable discussion, the esophagus approximately 5 cm. proximal to the papillary growth,

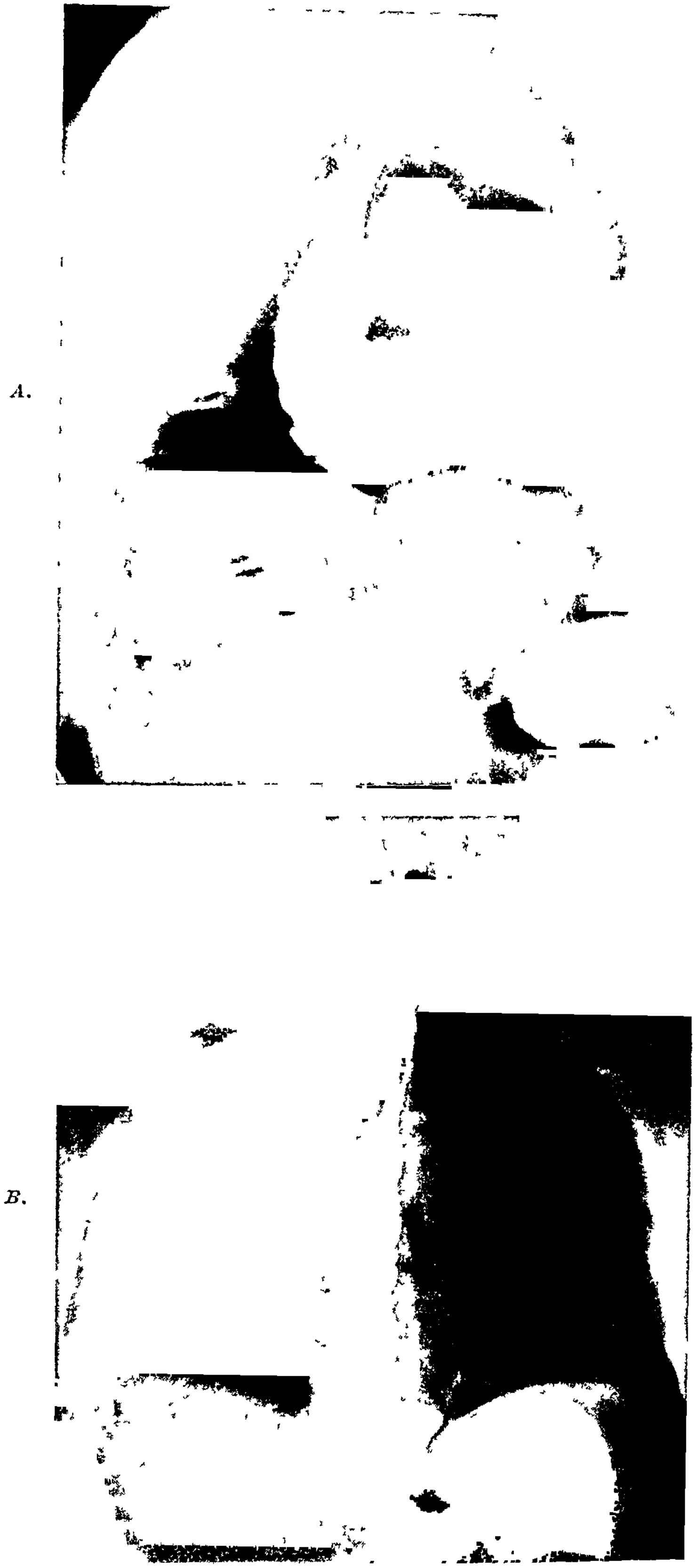

Fig. 1.—*A* and *B*, Chest roentgenograms showing hiatal hernia with stenosis of the distal esophagus (see text).

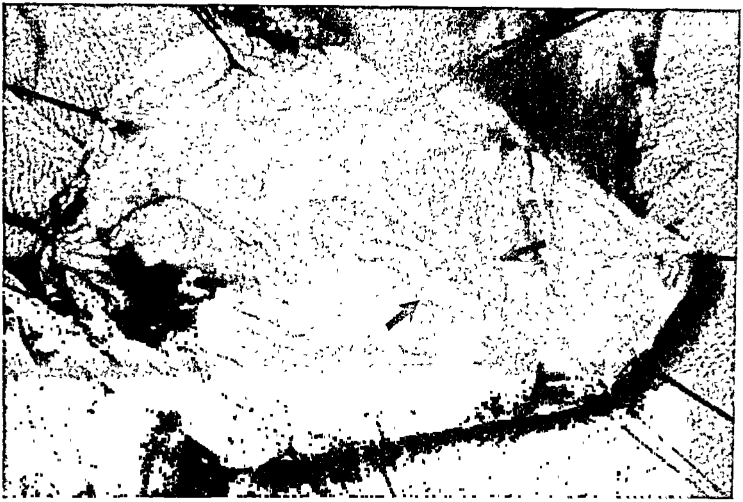

Fig. 2.—Photograph made at time of thoracotomy looking into the distal esophagus widely opened through a longitudinal incision. Arrows point to papilloma. Sites of earlier esophagoscopic biopsies are visible in adjacent area. Stenosed distal esophagus (cardioesophageal junction) is seen to reader's left; proximal esophageal lumen to the right (see text).

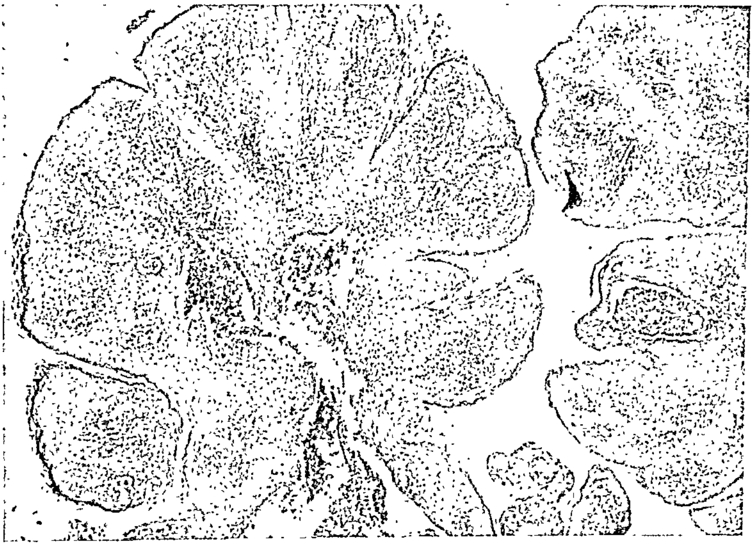

Fig. 3.—Photomicrograph of esophageal papilloma showing lobulated projections covered by well-differentiated squamous epithelium. There is a central core of fibrovascular tissue (see text further). (×20; reduced ⅙.)

and the stomach, distal to the site of stenosis, were resected. Gastroesophageal continuity was established by anastomosis of stomach to esophagus. A pyloroplasty was performed because of the vagectomy coincident with the esophageal transection. On gross inspection the surgical team could not be absolutely certain that malignant change did not exist in the base of this tumor. The patient's postoperative course was essentially uneventful and when last seen, 3 months following surgery, he was active and asymptomatic.

The pathology report* was as follows:

> The external surface of the surgically resected esophagus was not remarkable. On the mucosal surface, however, a soft papillary nodule with a broad base was noted. It measured approximately 0.8 cm. in diameter and projected about 0.3 cm. into the lumen. In close proximity to the papillary lesion a 0.4 cm. ulcer probably representing the site of a previous biopsy could be seen.
>
> Microscopic study on the sections revealed a papillary lesion with vascular fronds of connective tissue covered by well differentiated squamous epithelium. Parakeratosis and hyperkeratosis were present in the papillary projection but not elsewhere. There was no evidence of invasion into the broad pedicle. The lamina propria showed minimal lymphocytic infiltration.
>
> These sections are interpreted as a papilloma of the esophagus because of the true formation of papillary projections rather than artifactial folds. There is no evidence of a virus etiology since no inclusion bodies were present in the epithelial cells.

B. *Papilloma-like Esophageal Lesions With Distal Malignancy (4 Cases).*—

CASE 1.—J. D. (No. 66510), a 55-year-old white man, was admitted to the Roswell Park Memorial Institute on July 2, 1949, with the chief complaint of progressive dysphagia for 3 months. There had been a 40-pound weight loss during this period, and occasional regurgitation and aspiration had been noted. Barium esophagogram revealed an obstructing lesion in the lower esophagus. On esophagoscopy, a firm, granular mass was found obstructing the lumen, 36 cm. from the upper incisor teeth. No mention was made of esophagitis or mucosal hyperplasia. A biopsy was taken which was reported as showing papilloma of the esophagus. Because of the progressive obstruction, the patient had a thoracotomy performed. Carcinoma of the esophagus was found which was nonresectable because of local extension. A number of paraesophageal lymph nodes grossly involved with tumor were present. The patient died from his disease one month later and the diagnosis of carcinoma of the esophagus was confirmed on autopsy. No mention was made of any lesion resembling a papilloma in the proximal esophagus.

CASE 2.—C. J. (No. 65575), a 49-year-old white woman, was admitted to the Roswell Park Memorial Institute on March 28, 1949, with complaints of progressive dysphagia for 6 months. During this time she had lost 30 pounds. The only fact of significance in her past history was that she had had a complete hysterectomy and bilateral salpingo-oophorectomy in 1936 for a squamous-cell carcinoma of the uterine cervix. On physical examination there was a left vocal cord paralysis. Roentgenographic examination of the esophagus demonstrated an obstruction in the middle third of the esophagus thought to be due to carcinoma of the esophagus. Esophagoscopy revealed an esophageal obstruction, approximately 24 cm. from the upper incisor teeth, with rather prominent rolled mucosal folds on the posterior esophageal wall. This area was biopsied. The histologic examination was reported to be papilloma of the esophagus with marked thickening at the squamous epithelium and some cornification of the superficial cells. A repeat esophagoscopy one month later showed a similar obstruction by a mammillated mass on the posterior left lateral esophageal wall. A biopsy at this time was reported as showing thickened squamous epithelium and smears were negative for tumor cells. Because of the patient's poor general condition, no surgery was attempted and after a short course of radiation therapy she died. Unfortunately, no autopsy was obtained but a presumptive diagnosis of primary carcinoma of the esophagus was made The possibility that this obstructing neoplasm represented a uterine metastasis remains but seems rather unlikely

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*Reviewed by Dr. John Pickren, Chief of the Department of Pathology, Roswell Park Memorial Institute.

CASE 3 —B C. (No 73711), a 68 year old white woman, was admitted to the Roswell Park Memorial Institute on Dec. 12, 1951, because of progressive dysphagia and regurgitation of 7 months' duration. During this period she had lost 32 pounds Roentgenographic examination of the esophagus showed an irregular narrowing of the distal esophagus. At esophagoscopy, a raised, mammillated, ulcerated lesion in the left anterolateral esophageal wall was encountered, 37 cm from the upper incisor teeth This was biopsied and reported to be a papilloma of the esophagus At thoracotomy, an extensive carcinoma involving the lower esophagus and gastric cardia was found with metastases to the liver and celiac axis The patient died of her disease several months later without an autopsy being performed.

CASE 4 —A H (No 73761), a 73 year old white man, was admitted to the Roswell Park Memorial Institute on Dec 19, 1951, *complaining of progressive dysphagia for 3* months with a 7 pound weight loss. Radiographic examination of the esophagus showed an irregular narrowing in its middle third Esophagoscopy revealed an obstructing, ulcerated, friable lesion in the right lateral wall at a level 25 cm from the upper incisor teeth. The lesion was biopsied and reported to be a papilloma of the esophagus Esophagoscopy was repeated 3 weeks later with similar gross findings This time the lesion was described as a gray, glistening, papillary lesion obstructing the lumen and a biopsy was reported as showing papillary hyperplasia The patient was then subjected to exploratory thoracotomy and an advanced carcinoma of the esophagus was found and resected A plastic tube was used to re establish gastroesophageal continuity. Histologic section showed squamous cell carcinoma of the esophagus No mention was made of papilloma or esophagitis proximal to this area

Comment: Based upon histologic examination of the esophagoscopy biopsies, the last 4 cases were originally diagnosed as papilloma of the esophagus Unfortunately, a detailed description of the gross appearance of the lesion was not always recorded in the esophagoscopy reports In all 4 cases there was esophageal obstruction due to malignancy After re examining the original histologic sections and reviewing the clinical data, it is apparent that the mucosal lesions were areas of mucosal hyperplasia and papillary folding rather than true esophageal papillomas This will be discussed further

DISCUSSION

Perhaps a discussion of this subject should begin with a definition of the term papilloma of the esophagus Here one encounters what is possibly the basic difficulty in understanding and classifying the condition because the term papilloma has been loosely attached to a number of closely related esophageal lesions There often appears to be no uniformly clear line of division between a papilloma and a small sessile polyp, although a distinction may easily be made from the larger pedunculated adenomatous polyp Localized areas of epithelial hyperplasia and granulomatous proliferation have also been referred to as papillomas The issue becomes even more clouded in publications describing sessile intraluminal growths of the esophagus by the random use of such adjectives as papillary, polypoid, and wart-like

There is no apparent reason why papillomas could not occur in the human esophagus. The growth would be primarily of mucosal origin with a covering of squamous mucosa and a fibrovascular core derived from the underlying submucosa. It would appear as a sessile lobulated bud of variable size, somewhat similar to papillomas of the skin. The tumor should be differentiated from closely related lesions, such as localized areas of hyperkeratosis, acanthosis, and leukoplakia as well as sessile polyps.

With closer attention to the over-all gross appearance of the lesion and adjacent esophagus as well as to its histologic appearance, there may be less confusion in applying the proper terminology in the future. Certainly, the pathologist who examines either the piece of the tissue snipped free at esophagoscopy or else the postmortem esophagus with a partially digested, autolytic mucous membrane, is in a disadvantageous position to appreciate superficial intraluminal pathology.

Opinions concerning papilloma of the human esophagus have varied in recent years. Totten, Stout, and co-authors,[11] in discussing benign tumors and cysts of the esophagus, concluded that, "No instance of true papilloma, that is, warty epithelial growth, was encountered in human beings." Again in 1957 Stout[12] expressed a view that the cases reported as papilloma of the esophagus were not like lesions called papillomas in other parts of the body. He thought that the only lesions that could properly be called papilloma of the esophagus were the coral-like lesions consisting of central cords of fibrous tissue covered by stratified squamous mucosa which may be seen in the esophagus of cattle and swine. In these animals, a virus has been suggested as a possible etiologic agent. Palmer[8] considered esophageal papillomas as areas of localized epithelial hyperplasia, and he used the term epithelioma interchangeably with papilloma. The use of the term epithelioma is open to question because to some it carries a connotation of malignancy. In a general review of papillomas throughout the body, Wakeley[15] recently defined papilloma as "a branching or lobulated benign tumour derived from epithelium. This definition excludes inflammatory lesions, warts, and polypi." In discussing papillomas of the alimentary tract, he dismissed papilloma of the esophagus with the following sentence, "Papilloma of the esophagus is extremely rare." From such varying opinions one might conclude that not only is the nature of papilloma of the human esophagus unsettled, but also that there is still a question as to whether such a condition actually exists.

The case reported in this paper would appear to meet the necessary criteria to be called papilloma of the human esophagus. This opinion was reached only after careful consideration of its gross and microscopic appearance. It was a benign, sessile, lobulated tumor covered by squamous mucosa with a fibrous core. There was no evidence of mucosal folding, granulomatous proliferation, or leukoplakia.

In reviewing the cases reported as papilloma of the esophagus in the literature as well as our clinical material, certain common features were noted.

Essentially all were located in the distal esophagus, an area that is normally narrowed and one that may be subjected to the irritating effects of trauma, gastric reflux, and esophageal stasis. In all cases there was an esophageal obstruction or narrowing to a variable degree distal to the papillomatous lesions except one in which there was no x-ray study and the presence of esophageal narrowing was not mentioned. Thorough analysis of the reported cases was frustrated by the incomplete clinical and pathologic descriptions. Study of the esophagoscopic notes and other available information, however, suggests that many of these lesions were probably the result of inflammatory processes, irritation, or trauma with subsequent folded areas of mucosal hyperplasia and granulomatous masses. The case commonly cited by Jackson[4] as papilloma and originating in the upper esophagus with a long narrow pedicle was really a pedunculated fibroma and should not be considered a papilloma of the esophagus. The pathologic report was "Fibroma papillare."

The esophageal papilloma reported in this paper was associated with a hiatal hernia and stricture of the distal esophagus, presumably from esophagitis and scarring. To our knowledge hiatal hernia has not been noted previously in the literature on esophageal papilloma, but at the time when the earlier cases were reported hiatal hernia was the subject of little attention and could have escaped detection. Like the other cases of papilloma, in ours there was distal esophageal narrowing which could have led to stagnation, mucosal irritation, and esophagitis. One can only speculate as to what effect the products of stagnant decomposing foods had in the genesis of this growth.

Gastroesophageal reflux, so common with hiatal hernia, can produce a recurring form of esophagitis. Whether this is a major factor in the formation of papilloma of the esophagus remains conjectural. Palmer[8] feels that epithelial irritation is evident as the cause of most esophageal papillomas. In fact, he speaks of processes that lead to losses of epithelium which in turn result in hyperplasia of the remaining islets of cells. This condition is not truly analogous to the pseudopolyps seen with ulcerative colitis as has been suggested. The ulcers of reflux esophagitis involving squamous mucosa tend to remain shallow and are characterized by healing with recurrences. Stout[1] believes that lesions called esophageal papilloma in man are the result of inflammatory processes in which the esophageal lining has been thrown up into papillary folds. These papillary folds and granular areas could be mistakenly called papilloma by the pathologist who examines only the piece snipped off by esophagoscopic biopsy. The 4 cases diagnosed as papilloma from the esophagoscopic biopsy at this Institute in 1949 and 1951 were all found to be actually areas of epithelial hyperplasia with some papillary folding when reexamined in the light of current knowledge.

It becomes evident that the diagnosis of papilloma of the human esophagus is not easily made. To the radiologist observing the barium swallow or to the surgeon palpating the outside of an intact esophagus, a papilloma may remain unnoticed. Pathologists have mistakenly made a diagnosis of papilloma on the basis of an esophagoscopic biopsy. The experienced esophagoscopist, however, is in a position to help clarify any histologic misinterpretation by carefully describing the gross appearance of the tumor and noting any associated areas of fissuring, mucosal hyperplasia, leukoplakia, and esophagitis. A definite diagnosis of papilloma should only be made, however, when the surgically resected esophagus or fresh postmortem esophagus containing the tumor is carefully examined grossly and histologically.

The significance of papilloma of the esophagus remains unsettled. Of first importance is the danger that a diagnosis of papilloma based on esophagoscopic biopsy may divert attention from a more distal esophageal lesion that may be an unsuspected carcinoma. The papilloma itself has been considered to be a benign tumor that needs attention in only the rare case when it causes symptoms. Some, such as Palmer[8] and Wakeley,[15] consider this type of epithelial tumor to be a premalignant lesion. Terracol and Sweet[13] comment that malignancy resulting from an esophageal papilloma has been referred to as adeno-acanthoma. At this time one can only conclude that it is questionable whether this type of papilloma has any malignant potential.

It is beyond the scope of this paper to consider in great detail the histologic differentiation between papilloma and lesions with which it has been confused. Papilloma should not be confused with granulomatous proliferations and sessile glandular polyps. A papilloma may be readily differentiated from leukoplakia with its features of hyperkeratosis and epithelial atypism. Nevertheless, one cannot be absolutely certain that esophageal papilloma does not represent merely an advanced stage of localized epithelial hyperplasia or mucosal proliferation. The dividing lines between certain of these proliferating mucosal lesions may be vague in some cases and absolute definitions demand, at best, complete gross and histologic examination of the growth and the adjacent esophagus.

SUMMARY

Papilloma of the esophagus is an unsettled subject and one about which no unanimity of opinion exists. It is curious that interest in the subject has dropped in recent years despite the advances in esophagoscopy and thoracic surgery. Papilloma of the esophagus has been especially confused with localized areas of epithelial folding and mucosal hyperplasia. Granulomatous proliferations, leukoplakia, and sessile polyps should be more readily differentiated from papilloma. Complete gross and histologic examination of the resected esophagus and tumor may be necessary, however, before a definitive diagnosis may be reached.

A case of papilloma of the esophagus is reported. There was an associated hiatal hernia and stricture distal to the papilloma. The distal esophagus containing the tumor was resected. Four other cases originally diagnosed as papilloma of the esophagus on the basis of esophagoscopic biopsy are briefly described. This diagnosis was later shown to be incorrect. In these cases the papillomatous areas were encountered proximal to malignancies. Of

interest was the observation that practically all cases of papillomas of the esophagus, here and in the literature, occurred in the distal esophagus proximal to an obstructing esophageal lesion

Certain impressions gathered from this review are discussed Absolute conclusions concerning the nature of papilloma of the human esophagus can not be reached at this time, but variances in opinion are cited along with the findings in our clinical material Perhaps as more attention is directed to the lower esophagus by clinicians and pathologists, the true nature of papilloma and related sessile mucosal lesions may become better understood

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TRANSIENT PARADOXICAL MOVEMENT OF THE DIAPHRAGM

Raymond A. Gagliardi, M.D., Howard H. Feigelson, M.D., and
Arthur S. Shufro, M.D., Detroit, Mich.

PARADOXICAL motion of the diaphragm following phrenicotomy or on the basis of malignant involvement of the mediastinum is a well known and familiar entity. The fact that paradoxical motion of the diaphragm can occur in the presence of nonmalignant pulmonary disease or without direct phrenic involvement is less well known. In view of this latter observation, it is felt justified to review the literature regarding this phenomenon and to consider the possibility of unilateral diaphragmatic paralysis occurring secondary to inflammatory disease of the lung.

In 1898, only 3 years after the discovery of the roentgen ray, Kienbock[1] described a case of hydropneumothorax in which the air-fluid level was noted to descend on expiration and to ascend on inspiration. He first coined the phrase "paradoxical movement of the diaphragm" and this change has become known as Kienbock's phenomenon. When first observed it was erroneously felt that the change was on the basis of the weight of the fluid in the pneumothorax cavity. Since that time, multiple causes have been implicated. The commonest cause of unilateral paralysis of the diaphragm is phrenicotomy or phrenic crush. Any other involvement of the phrenic nerve or its centers in the cervical spinal cord can produce the same phenomenon. Poliomyelitis with involvement of the anterior horn cells of the fourth cervical segment and injuries to the cervical cord are possible causes of central paralysis affecting the diaphragm. Involvement of the hilum of the lung by neoplasm with infiltration of the phrenic nerve is perhaps the commonest cause of diaphragmatic paralysis in which the peripheral portion of the phrenic nerve is involved. Cases have been described in which paralysis of the diaphragm developed during the course of pulmonary tuberculosis, apparently secondary to involvement of the phrenic nerve by scar tissue. A single case of diaphragmatic paralysis secondary to involvement of the phrenic nerve by an adjacent aortic aneurysm has also been described.[2] In all these cases, however, a true paralysis of the diaphragm, which is irreversible, was not present.

In 1929, Bonorino and Vadone[3] performed an exhaustive study to determine the mechanism of the Kienbock phenomenon. Their work showed that

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From the Departments of Radiology, Sinai Hospital of Detroit, and Wayne State University College of Medicine, Detroit, Mich.

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paradoxical motion of the diaphragm may occur in the absence of direct involvement of the phrenic nerve. They noted that in the presence of pneumothorax, when the intrapleural pressure at expiration was negative, the motion of the diaphragm was always normal. As the intrapleural pressure was increased from negative to positive there was a gradual change in the motion of the diaphragm which became paradoxical when the intrapleural pressure became positive. They further demonstrated that when the intrapleural pressure was at zero or only slightly above, there was normal diaphragmatic motion with the patient standing erect but the motion became paradoxical when the patient would lie on the side of pneumothorax. This work has been confirmed many times and is a simple method to determine whether or not a positive pressure pneumothorax exists.[5] It also demonstrates, unequivocally, that paradoxical *motion of the diaphragm may occur without involvement of the phrenic nerve.*

Upward displacement of the diaphragm in pneumonia was reported by Wu in 1932,[4] who felt that this was due to diaphragmatic failure to descend during deep inspiration secondary to loss of expansibility of the consolidated portion of the lung. This finding was further pursued by Friedman[7] in 1950, who followed, with fluoroscopy, a group of patients with pneumonia who also had elevated diaphragms. He reports 6 well studied cases of unilateral paralysis of the diaphragm which occurred in association with pneumonia. These paralyses all occurred on the same side as the pneumonia. In one of these cases there was concomitant vocal cord paralysis. He describes the onset of paralysis as occurring coincidentally with the pneumonia in 2 of the cases but in the remaining 4 there was a latent period of over 5 weeks between the onset of the pneumonia and the appearance of the paradoxical motion of the diaphragm. Paralysis lasted from 7 weeks to 10 months and in one case was apparently permanent. It was his feeling that the paradoxical motion of the diaphragm was secondary to paralysis of the phrenic nerve because of a toxic or inflammatory neuritis. On the basis of this work by Friedman, we present a recent case of pneumonia with paralysis of the diaphragm which was completely studied and carefully followed. This represents an additional case of paralysis of the diaphragm following a pneumonia to be added to the 6 cases of Friedman which are the only cases of this type we have been able to find in the literature.

CASE REPORT

H. S. (case reported through the courtesy of Dr. Aubrey Goldman), a 44 year old white man, was admitted to the Sinai Hospital of Detroit on Sept. 28, 1957. The patient had been well until 4 weeks before admission when he felt fatigue and malaise. One week later he complained of continued malaise and was seen by his physician who found rales at the base of the left lung and a temperature of 102° F. Roentgenograms at that time showed left lower lobe pneumonia with elevation of the left diaphragm (Figs. 1 and 2). One week later, repeat roentgenograms showed clearing of the pneumonia, and fluoroscopy demonstrated paradoxical motion of the left diaphragm, accentuated by sniffing. Since the onset of his illness he had lost 7 pounds in weight. He was admitted to the hospital for further evaluation. Repeat fluoroscopy on admission again demonstrated the paralysis of the left diaphragm

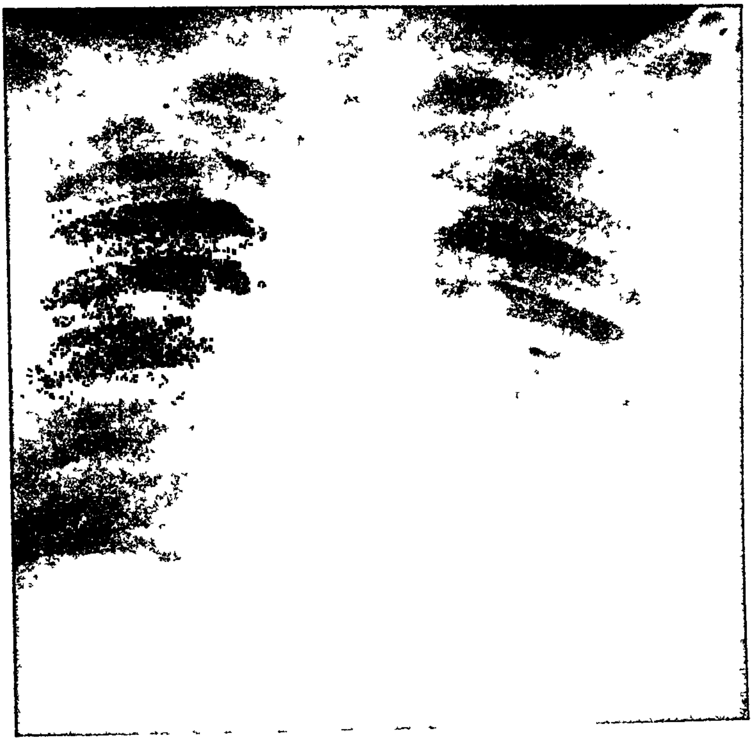

Fig. 1.—Left hemidiaphragm elevated with paradoxical motion demonstrated at fluoroscopy.

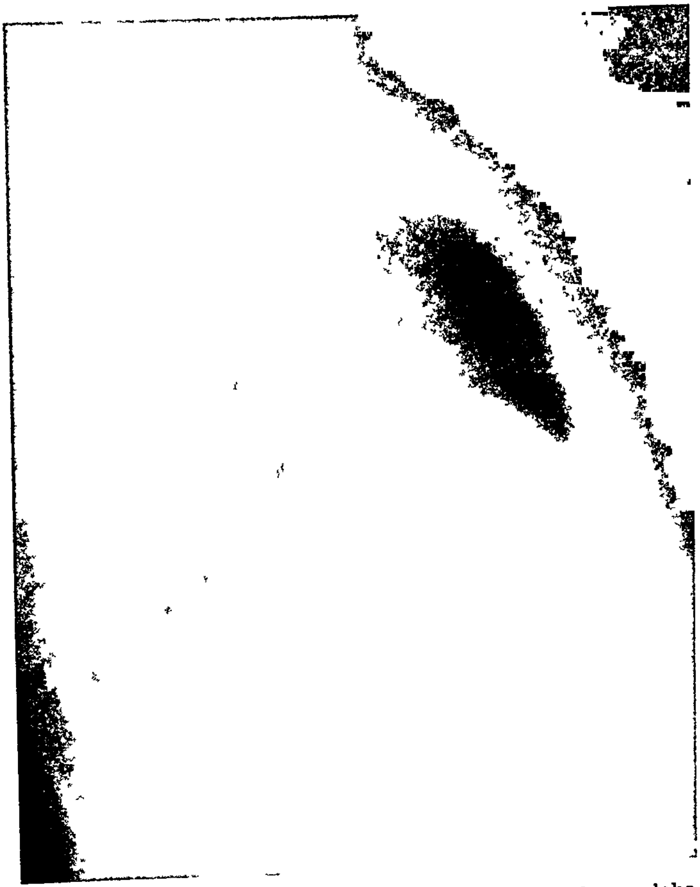

Fig. 2.—Elevation of left hemidiaphragm with adjacent left lower lobe pneumonia.

Significant in his past history was a bilateral dorsolumbar sympathectomy done 7 years earlier for hypertension. At that time, both roentgenograms and fluoroscopy of the chest were reported as normal. There had been no other chest x-ray studies in the intervening years.

Planigrams of the chest were normal. Bronchoscopy on Oct. 2, 1957, showed probable compression of the left main bronchus by an extrinsic tumor. On October 4, bilateral scalene node biopsy was done demonstrating only sinusoidal hyperplasia. On Oct. 8, 1957, a repeat bronchoscopy was done by a different observer who also reported an extrinsic deformity of the left main bronchus. Bronchial washings from both bronchoscopic examinations were negative. Biopsy of the left main bronchus showed chronic bronchitis with no evidence of malignancy. On Oct. 15, 1957, an exploratory thoracotomy was performed. Careful exploration of the mediastinum and hilum revealed no tumor with no anatomic reason for phrenic paralysis. Aside from transient urinary retention, the postoperative course was uneventful. Repeat fluoroscopic examination on October 23 still showed some diaphragmatic elevation but the motion was normal. The return to normal was 8 weeks after the onset of the disease or 7 weeks after the diaphragmatic abnormality was first detected.

DISCUSSION

It is possible that unilateral paralysis of the diaphragm occurs more frequently than generally suspected since most cases of pneumonia are examined without the aid of fluoroscopy. The physical signs of diaphragmatic paralysis are easily missed or overshadowed by adjacent changes, especially in the presence of pulmonary inflammatory disease. The diagnosis of paralysis of the diaphragm is made on the basis of elevation of the diaphragm as well as paradoxical movement at fluoroscopy. If the patient is asked to sniff sharply, the paradoxical motion is accentuated.

Elevation of the diaphragm may be due to subdiaphragmatic disease such as a subphrenic abscess with mechanical upward displacement of the diaphragm. It may also occur in the presence of severe chest pain or pleural pain or, in pneumonia, due to the loss of expansion as described by Wu. It may also occur as previously described in the presence of a high positive pressure pneumothorax during inspiration. Eventration of the diaphragm may also demonstrate paradoxical motion but this is not a reversible process. In the case described, careful fluoroscopic observation was felt to rule out the possibility of a subphrenic abscess as well as limitation of motion due to chest pain. There was no evidence of pneumothorax, and the previous history of fluoroscopy by a competent observer ruled out the possibility of an eventration of the diaphragm. The diagnosis, therefore, lay between involvement of the phrenic nerve by an occult carcinoma or changes secondary to pneumonia.

The physical reasons for the occurrence of paradoxical motion of the diaphragm in the absence of definitely demonstrable mechanical involvement of the phrenic nerve are not clear. This is especially true since the problem of thoracic dynamics is a complicated one with many interlocking factors. We may note, however, the mutual dependence between the muscular action of the diaphragm and the elastic action of the lung. The contracting diaphragm at inspiration distends the lung and on expiration, when the diaphragm is relaxed, the force of the lung's elastic retraction causes the diaphragm to rise. It would appear that any interference in the action of the elastic force of the lung would modify the mechanical relationship between the diaphragm and the lung. This suggests a possible mechanical explanation to supplement the implication of toxic involvement of the phrenic nerve in intrathoracic pulmonary disease. We feel that this condition may be relatively common. Since paralysis of the diaphragm is apparently delayed and may not occur until after the pulmonary findings have completely cleared and because paralysis of the diaphragm is asymptomatic, it may not be investigated. It is our plan to follow future cases of pneumonia with fluoroscopy for a better evaluation of the problem of delayed diaphragmatic paralysis.

SUMMARY

A brief review of the literature is presented regarding the multiple possible explanations for paradoxical motion of the diaphragm.

A case is presented in detail in which paralysis of the diaphragm occurred concomitantly with pneumonia and which subsided after a period of 8 weeks. The possibility of inflammatory involvement of the phrenic nerve as a cause of diaphragmatic paralysis is suggested.

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LEIOMYOMA OF THE DIAPHRAGM

Jesse H. Meredith, M.D., and H. H. Bradshaw, M.D.,*
Winston-Salem, N. C.

TUMORS of the diaphragm are rare. Reviews and collections of cases in the literature have been made by Clagett and Johnson[1] in 1949, and Samson and Childress[2] in 1950. The total number reported was thirty-five. Since then there have been scattered reports of these lesions,[3-14] which makes a total of forty-two. One half were malignant and only one was of smooth muscle origin, a leiomyosarcoma.[3] This report is submitted to re-emphasize the use of pneumoperitoneum as a convenient diagnostic aid to roentgenography in the study of these shadows, and to draw attention to the incidence of malignancy in tumors of the diaphragm.

CASE REPORT

A 57-year-old woman was admitted to the North Carolina Baptist Hospital on Sept. 22, 1955, because of a progressively enlarging shadow in the left lower portion of the chest. Two previous annual films were interpreted as representing elevation of the diaphragm. She was entirely asymptomatic and review of the other systems showed no abnormality. There were dullness and absence of breath sounds in the left lower chest; the diaphragm descended on inspiration. Posteroanterior and lateral chest films (Fig. 1) showed the shadow above the diaphragm. A 1,500 c.c. pneumoperitoneum, given in 500 c.c. stages, demonstrated a normal contour of the inferior surface of the diaphragm (Fig. 2), above which there was a mass that could not be differentiated from the diaphragm. The usual laboratory studies were normal.

On September 27, through the bed of the left eighth rib, the thorax was explored and a 17 by 14 by 18 cm. mass was found in the lower portion of the chest (Fig. 3). It arose from the diaphragm by a 6 cm. area and was adherent to the inferior surface of the lung. The major portion of the blood supply to the tumor came from a large vessel that arose from the abdominal side of the diaphragm. The tumor was resected along with a 2 cm. full thickness margin of apparently normal diaphragm. The defect was easily closed with interrupted sutures of silk. The pathologist's diagnosis was "leiomyoma of the diaphragm." There was no evidence of malignancy (Fig. 4). The postoperative course was uneventful; she was discharged on the eighth postoperative day and has been observed for 3 years without evidence of recurrence.

DISCUSSION

Tumors of the diaphragm are usually asymptomatic and discovered as incidental findings on roentgenograms of the chest. Of the few that have

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From the Department of Surgery, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C.

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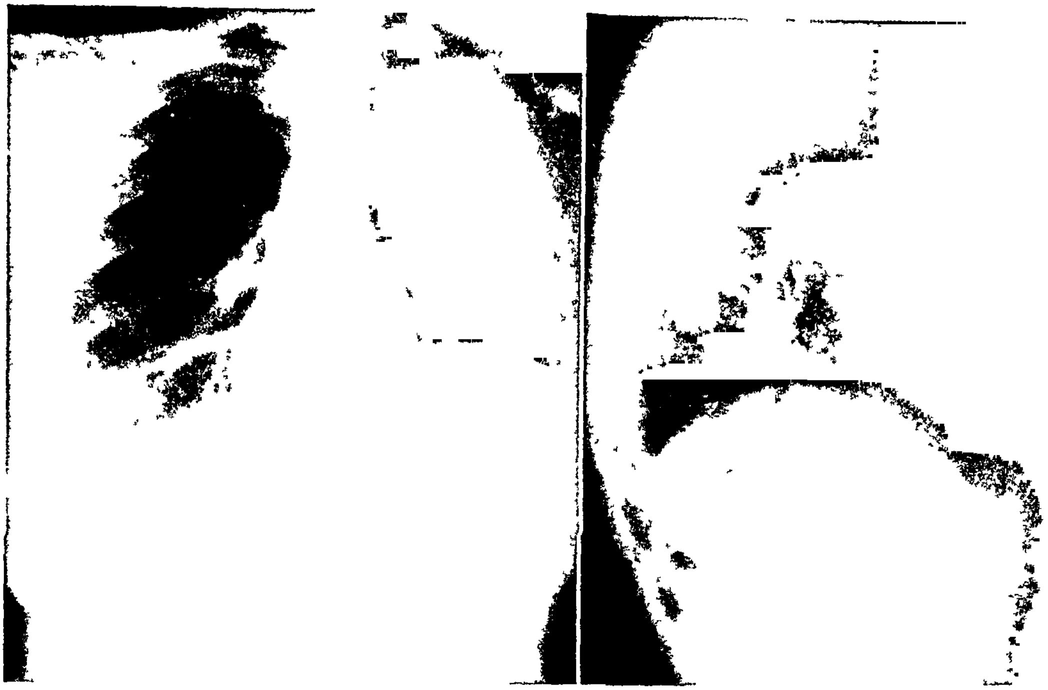
*Research Fellow, National Heart Institute, National Institute of Health, Bethesda, Md.

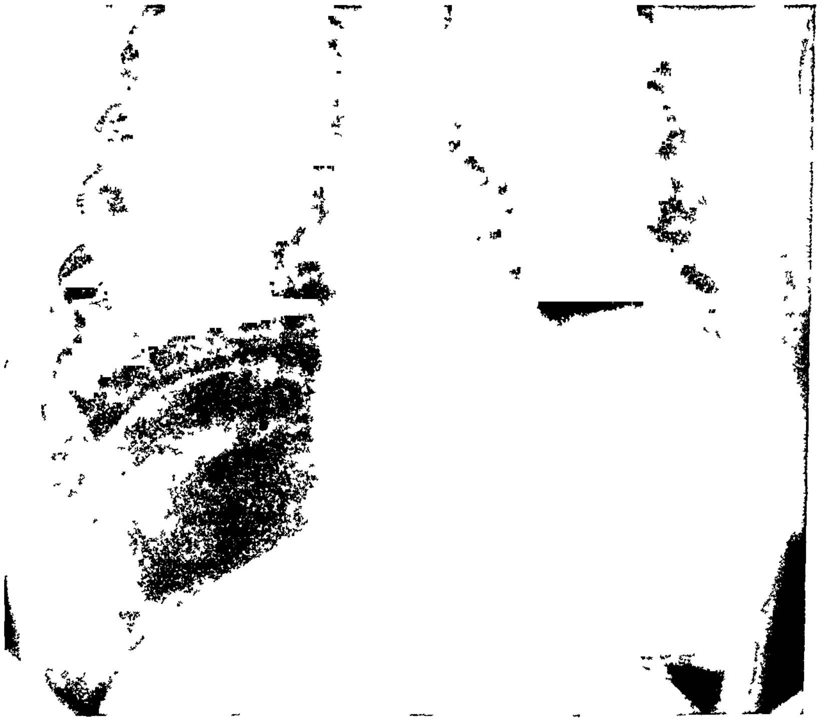


A

B.

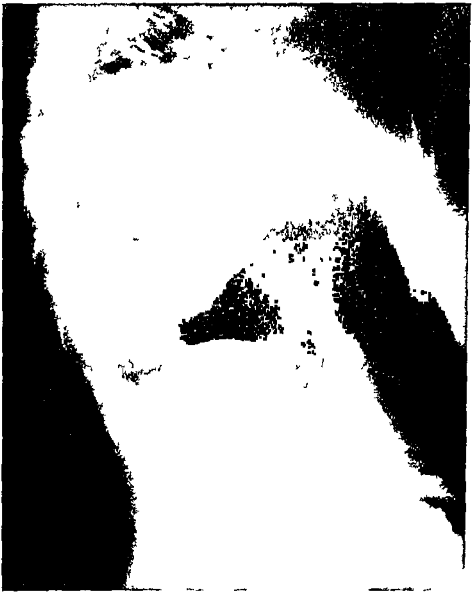
Fig. 1.—A. Posteroanterior film of the chest. Apparent elevation of the left hemidiaphragm is shown.

B. The apparent elevation is also present. The tumor is seen to not extend anteriorly as far as is expected of the diaphragm.



A

Fig. 2.—A. Posterolateral view with pneumoperitoneum demonstrating the tumor well.



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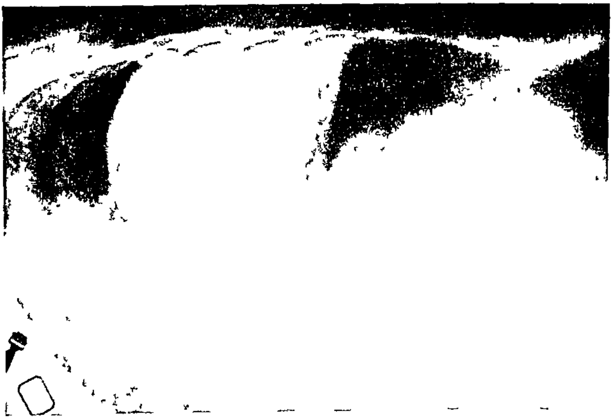

C

Fig 2.—Cont'd *B* Lateral view with pneumoperitoneum The mass below the diaphragm is the spleen

C, Anteroposterior view with the patient on the right side and made with horizontal beam in the presence of pneumoperitoneum

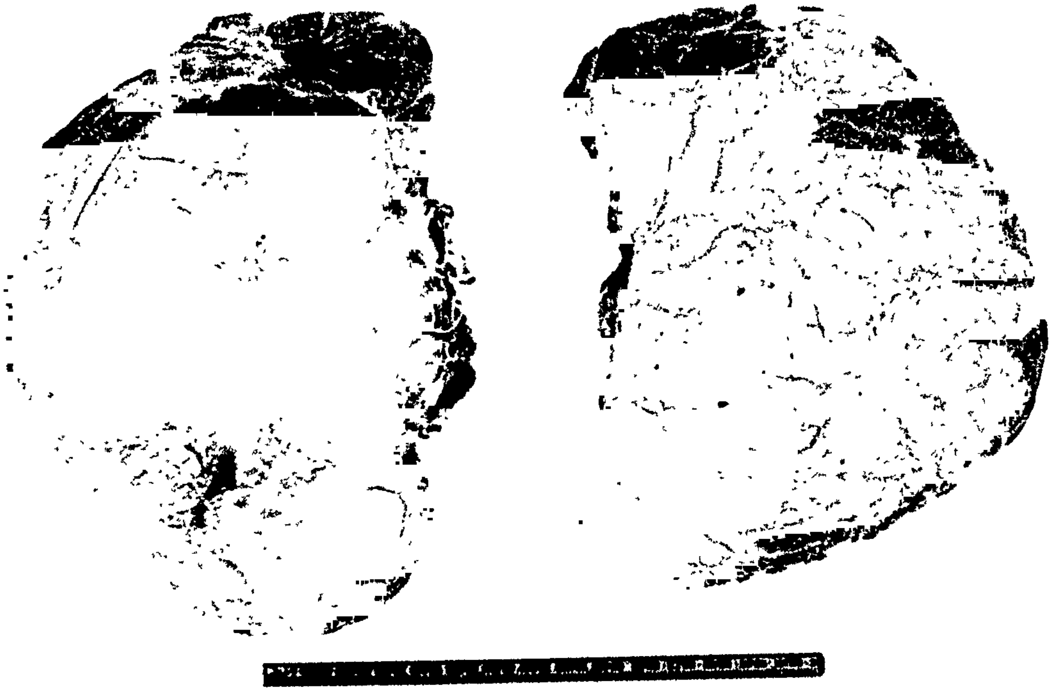

Fig. 3.—Photograph of the leiomyoma. The left view is of a surface and the right of a central section. The pedicle is easily seen.

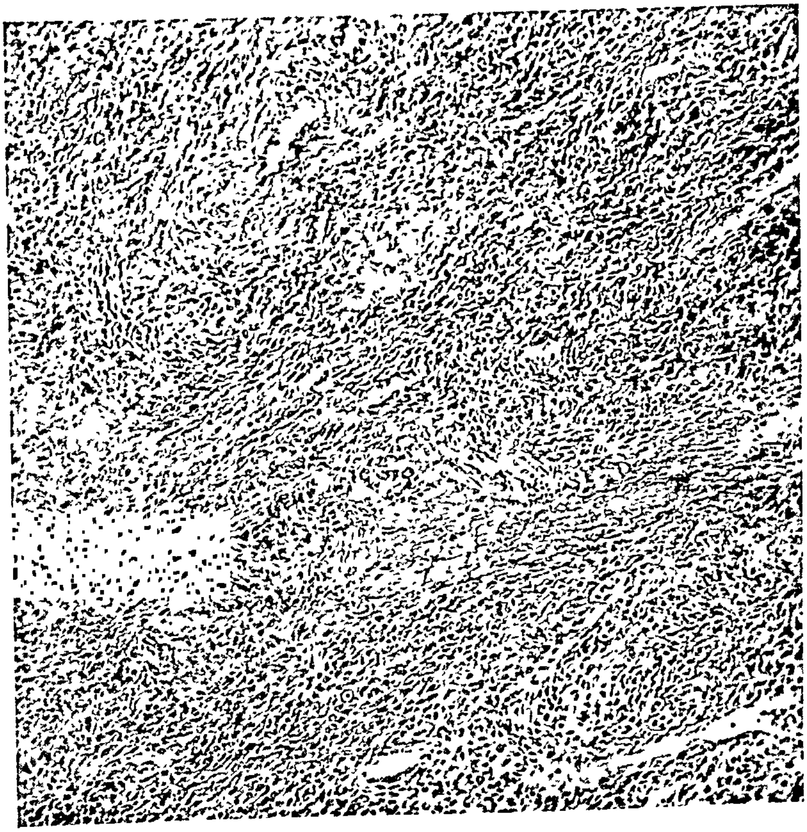

Fig. 4.—Photomicrograph of the leiomyoma.

caused symptoms, the most common complaints are those of pulmonary dysfunction due to displacement of the lung by large lesions[2] The lesion in point was large but asymptomatic A definite diagnosis is, of course, not possible until exploration of the chest and histologic studies are complete Studies which define the lesion as one of the diaphragm should be attempted In addition to the usual films of the chest the most satisfactory procedures are fluoroscopy, pneumoperitoneum,[4] and pneumothorax The former two were used in this case and by far the more information was gained from intraperitoneal air The value of pneumothorax may be limited by adhesions to the inferior surface of the lung Early treatment by resection is the treatment of choice and is usually easily accomplished Closure of the defect can be enhanced by preoperative pneumoperitoneum and/or crushing of the phrenic nerve[6] The fact that one half of the tumors of the diaphragm are malignant should be kept in mind when a tumor in this area is encountered and a wide margin of apparently normal tissue removed with it

SUMMARY

A leiomyoma of the diaphragm was discovered accidentally during a chest film survey It was resected without difficulty The need of early diagnosis and treatment of mass lesions of the diaphragm is stressed The value of pneumoperitoneum both as an aid to diagnosis and to closure of the defect following resection is re emphasized

ADDENDUM

Six months after submission of this manuscript for publication, roentgenograms of the chest revealed a lesion of the right upper lobe This lesion has been resected and is a "spindle cell malignant tumor" It is the opinion of the pathologist and the authors that this is a metastasis from the previously reported lesion

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THE VALUE OF BRONCHOSCOPY IN DETERMINING THE INOPERABILITY OF CARCINOMA OF THE LUNG

Edward B. Benedict, M.D., Boston, Mass.*

BRONCHOSCOPY is well recognized as an important procedure in the diagnosis of cancer of the lung because it frequently leads to a positive biopsy and to the aspiration of secretions for cytologic study.[1] Bronchoscopy is less well established but of almost equal importance because of the information it may give regarding the chance of successful resection of the tumor. Over and over again the question arises as to whether or not a bronchogenic carcinoma can be surgically removed. Unfortunately, most patients with cancer of the lung are *incurable* when first seen. However, the primary tumor may still be *resectable* and the patient benefited by such palliative resection. If all the evidence suggests that a tumor cannot be resected, exploratory thoracotomy can be avoided. Many factors enter into the decision, including age and general condition of the patient, x-ray studies, angiocardiography[2] and last, but not least, the bronchoscopic findings.

BRONCHOSCOPIC FINDINGS WHICH USUALLY MEAN INOPERABILITY

It should be emphasized that a physician or surgeon who does only an occasional bronchoscopy is not competent to evaluate the sometimes difficult aspects of bronchoscopic interpretation. Much experience is necessary. The following points are of special importance.

Location of Tumor.—If the lesion involves the trachea, the chance of successful resection is small.

Carina.—Widening and fixation of the carina usually mean that the tumor has invaded the mediastinal glands to such an extent that it cannot be removed.

Fixation.—If the bronchus is fixed in the region of the carcinoma, it often means peribronchial invasion of such a degree as to mean unresectability.

Angulation.—Extrinsic pressure frequently causes abnormal angulation of the bronchus probably due to metastatic glands or local extension of the growth, making resectability unlikely.

From the Surgical Services, Massachusetts General Hospital, and the Department of Surgery, Harvard Medical School, Boston, Mass.

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*Assistant Clinical Professor of Surgery, Harvard Medical School; Endoscopist, Massachusetts General Hospital.

Narrowing of the bronchus may mean infiltration of the bronchial wall by carcinoma or extrinsic pressure from local extension of the tumor or from metastatic glands. If this is accompanied by some fixation it may mean unresectability.

In reviewing a series of 3,247 bronchoscopies in the 12-year period, 1946-1957, I have found 147 cases of proved bronchogenic carcinoma which I thought were probably inoperable, by which I meant that the chances were against satisfactory surgical removal. One hundred and twenty of these patients were not explored. In spite of the bronchoscopist's adverse opinion, 28 patients were subjected to exploratory thoracotomy and were found to be unresectable in 17 instances. In 8 others, the resection was of doubtful value.

GROUP I. PATIENTS CONSIDERED PROBABLY INOPERABLE BY BRONCHOSCOPY—NOT OPERATED UPON

One hundred and twenty cases belong in this group. Some of these were obviously poor-risk patients from the point of view of age, general condition, and x-ray findings, but in many of them the additional evidence of probable inoperability by bronchoscopy was one of the most important factors in the decision against surgery.

GROUP II. PATIENTS CONSIDERED PROBABLY INOPERABLE BY BRONCHOSCOPY, SUBSEQUENTLY EXPLORED AND FOUND TO BE UNRESECTABLE

Seventeen cases fall into this category and were found to be inoperable for various reasons as follows: "tumor surrounded pulmonary artery," "very large malignancy surrounding the hilum and attached to pericardium," "fixation and widespread involvement of lymph nodes," "hilum full of large nodes, adherent mediastinum," "sclerosing mass of carcinoma found in hilum." For detailed comparison of bronchoscopic findings with surgical findings see Table I.

GROUP III. PATIENTS CONSIDERED PROBABLY INOPERABLE BY BRONCHOSCOPY, SUBSEQUENTLY *RESECTED WITH POOR RESULTS*

In eight of these cases, surgery was undertaken and pneumonectomy accomplished in 6, lobectomy in 2. One of the pneumonectomy patients died 12 days postoperatively of severe bronchitis with mucus plugs, bronchopneumonia, and hypertensive heart disease. One of the lobectomy patients was an asthmatic who tolerated surgery so badly that pneumonectomy could not be performed, and an "adequate cancer operation could not be done." This patient died of recurrence 5 months after the operation. Three of the pneumonectomy patients died of recurrence 3, 5, and 8 months, respectively, after surgery. A third pneumonectomy patient looked badly and had no energy 7 months after surgery with large, probably recurrent, nodules in the scar. Of the 2 patients who had the longest postoperative survival, one (lobectomy) died of recurrence in 1 year and 4 months, and the other (pneumonectomy) died of

TABLE I (GROUP II)

	REASON "PROBABLY INOPERABLE" BY BRONCHOSCOPY	REASON INOPERABLE AT THORACOTOMY
Case 1	Cancer involving right upper lobe, right intermediate bronchus with extrinsic pressure on right side of trachea	Tumor surrounded pulmonary artery
Case 2	Cancer of left upper lobe, with narrowing, angulation, and fixation of left main bronchus	Very large malignancy adherent to chest wall, surrounding the hilum and attached to pericardium
Case 3	Complete stenosis of right upper lobe, fixation in that area and evidence of extrinsic pressure	Because of fixation and widespread involvement of lymph nodes
Case 4	Findings consistent with cancer of left main bronchus, close to carina, much fixation	Hilum full of large nodes, adherent mediastinum
Case 5	Bronchogenic cancer involving entire main bronchus and probably extending as high as carina, probably inoperable because of location, fixation, and widening of mediastinum	Sclerosing mass of cancer found in hilum with an outcrop of the disease in fungating form in the pleural cavity, posteriorly
Case 6	Cancer involving right upper lobe, lower end of trachea, right main bronchus and right intermediate bronchus, extrinsic pressure and fixation, almost certainly inoperable	Inoperable because of chest wall and mediastinal invasion
Case 7	Carcinoma left main bronchus, very close to carina, probably invading mediastinum and probably inoperable	Inoperable, primary tumor arose in left upper lobe near the hilus and all lymph node bearing areas were apparently invaded by carcinoma
Case 8	Cancer involving the left main and left lower lobe bronchi causing some fixation	Because it revealed a stony hard mass involving hilum
Case 9	Widening, deviation, and fixation of carina and mediastinum, narrowing of the right main bronchus and right intermediate bronchus with fixation, narrowing and stenosis of the right upper lobe orifice, probably due to inoperable carcinoma	Hard mass in the right upper lobe with extensive nodal involvement around the main bronchus in the subcarinal area and in the mediastinum extending up almost to the base of the neck
Case 10	Cancer right main bronchus, right upper lobe orifice, right intermediate bronchus, probable invasion of mediastinum and peribronchial glands	Extended to encompass right pulmonary artery and superior pulmonary vein and superior vena cava
Case 11	Left lower lobe bronchus markedly deviated as if from pressure on mediastinal side	Fluid in chest, left lower lobe completely atelectatic, large mass with nodules extending around aorta in region of hilum
Case 12	Paralysis of vocal cord, cancer lower end of left wall of trachea	Invasion by carcinoma too complex
Case 13	Cancer lower end of trachea, right main bronchus and complete obstruction of right upper lobe orifice, some fixation	Large mass involving right upper and middle lobe invading superior vena cava
Case 14	Extrinsic pressure lower trachea and right main bronchus and right intermediate bronchus, some mediastinal widening	Matted lymph nodes in hilus of lung surrounded upper lobe and extending across trachea, metastatic carcinoma wall of vena cava

TABLE I.—CONT'D

	REASON "PROBABLY INOPERABLE" BY BRONCHOSCOPY	REASON INOPERABLE AT THORACOTOMY
Case 15	Left main bronchus rather fixed on both sides apparently by a mass in the mediastinum and a mass in the left upper lobe, marked angulation left upper lobe, bronchus narrowed about 1 cm. inside the orifice	Tumor left upper lobe invading arch of aorta at the region of the recurrent laryngeal nerve
Case 16	Cancer involving left main bronchus, much fixation and displacement	Upper lobe completely solid and filled with tumor, lower lobe atelectatic, tumor overlay arch of aorta and was firmly in lobules around all of the structures of the hilum
Case 17	Cancer of the right main bronchus close to the carina	Firm mass in region of the hilum of the lung and numerous enlarged obviously invaded lymph nodes extending up the mediastinum behind the superior vena cava to the apex of the chest

recurrence in 1 year and 10 months. Obviously these results are not good and may indicate no greater palliation or survival period than might have been obtained by x-ray treatment, nitrogen mustard, or even no treatment at all.

GROUP IV. PATIENTS CONSIDERED PROBABLY INOPERABLE BY BRONCHOSCOPY, SUBSEQUENTLY RESECTED WITH GOOD RESULTS

Two cases fall into this category and represent bronchoscopic misinterpretation. One of these occurred early in the series (1946) in a patient thought to be probably inoperable because of angulation and fixation of the left main bronchus with paralyzed right vocal cord. Fortunately, in this patient, the radiologist had reported only a "collapse of the anterior inferior segment of the left upper lobe probably due to bronchogenic carcinoma." At the time of surgery by Dr. R. H. Sweet, a left pneumonectomy was accomplished and the patient is alive and well now, 12 years later. This bronchoscopic error was explained at operation as being due to severe acute pneumonitis with a large number of enlarged lymph glands at the left hilum. The recurrent laryngeal nerve was not involved. The pathologic report was epidermoid carcinoma grade 3, chronic pneumonitis, regional nodes negative for carcinoma.

The other patient, alive and well 7 years after pneumonectomy by Dr. Gordon Scannell, represents a mistaken evaluation by bronchoscopy, where, because of marked angulation, narrowing, and fixation, I thought the tumor was—"probably invading the mediastinum. My impression is that it is probably inoperable. If surgery is to be attempted, I believe pneumonectomy would be necessary." The x-ray interpretation was "primary bronchogenic tumor of the left upper lobe, enlargement of at least nodes in the left lung root." The surgical consultant made the following excellent evaluation, "Both the x-ray studies and bronchoscopy report are unfavorable as regards operability. Both of these methods of evaluation, however, are not 100% reliable in this regard because superimposed infection may contribute to the observed changes. For these reasons and because alternative methods of treatment offer so little I would not consider this lesion inoperable without a thoracotomy.'' The assistant resident also noted, ''this man is so 'well' and in such good condition generally that he should have every possible opportunity for definitive surgery.'' At the operation a ''large nodular tumor was encountered in the medial aspect of the left upper lobe involving the pulmonary artery close to its emergence from the mediastinum. Therefore, an intrapericardial approach was used and the left pulmonary artery, left superior pulmonary vein and inferior pulmonary vein secured without difficulty at this level. . . . Excellent exposure was obtained throughout, and it was unlikely that a resection could have been done unless this were done intrapericardially, but at this level the exposure and the ease of access were entirely satisfactory.''

DISCUSSION

The physician or surgeon who is treating cancer of the lung would like to know as certainly as possible whether or not it is worth while to offer his patient exploratory thoracotomy. Many factors are involved in the decision, including the patient's age and general condition, the x-ray appearance of the tumor, the patient's willingness to undergo major surgery, and sometimes the angiocardiographic findings. Very often the surgeon expects no more than palliation even from a pneumonectomy. Definite help can be obtained from bronchoscopy. In 120 out of the 147 cases in this series (81.6 per cent), the bronchoscopic study plus the physical and x-ray findings were so unfavorable that surgery was not done. In 17 other cases (11.6 per cent), the bronchoscopic report was unfavorable but exploratory thoracotomy was performed anyway and the tumor proved to be unresectable. In 8 cases (5.5 per cent), resection was possible in spite of the unfavorable bronchoscopic report; however, the surgical result was poor both as regards palliation and length of survival. In the remaining 2 cases (1.4 per cent), the bronchoscopist's judgment was incorrect and the tumor was resected with a very good result.

CONCLUSIONS

In experienced hands, bronchoscopic evaluation of the extent of bronchogenic carcinoma and its probable inoperability is very important.

In this series of 147 cases, the bronchoscopic accuracy, as regards inoperability, was 98.6 per cent.

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A SIMPLE METHOD FOR THE INDUCTION OF TOPICAL LARYNGO-TRACHEO-BRONCHIAL ANESTHESIA

Thomas E. Starzl, M.D., and Edward P. Cruzat, M.D., Chicago, Ill.

IN the past we have performed diagnostic bronchoscopy on a group of paraplegic patients in whom the induction of topical anesthesia in the usual way was difficult. For these patients, a method of applying local anesthesia was developed which was so effective and simple that it has become our preferred technique in the preparation of all adult patients for endoscopy or bronchography. Anesthetization can be done very quickly and effectively. This method has been used approximately 150 times with no major or minor complications.

METHOD

The patient may be either lying or sitting. A No. 12 or 14 plastic catheter is passed into the trachea by the nasotracheal route in the same way as if nasotracheal suction were to be carried out.[1] No difficulty will be encountered in passing the catheter if it is advanced slowly until the tip lies just above the glottis as judged by the passage of air through the catheter with each respiration. The tip is then quickly passed into the upper trachea when the patient coughs or takes a deep breath (Fig. 1, *A*). At this time some patients will have paroxysmal coughing so that it is necessary to have the local anesthetic ready for immediate instillation. A syringe is attached to the catheter, and 3 to 5 c.c. of 5 per cent cocaine is injected slowly over a 5-minute period, taking care that the plunger is firmly held (Fig. 1. *A*) to prevent its expulsion from the syringe barrel. When the first portion of the cocaine is injected. coughing is induced but the cough reflex is rapidly obtunded after the first 1.0 c.c. or so of cocaine has been instilled.

If bronchograms are to be obtained, the catheter is placed in position under fluoroscopy. If bronchoscopy is the objective, the catheter is withdrawn and the bronchoscope can be passed immediately. In either [illegible] anesthesia is excellent. No additional hypopharyngeal anesthesia is [illegible] since the cocaine is coughed up into this area from the tracheal [illegible] instillation (Fig. 1, *B*).

From the Department of Surgery, [illegible] University Medical School [illegible] erans Administration Research Hospital, Chicago, Ill.

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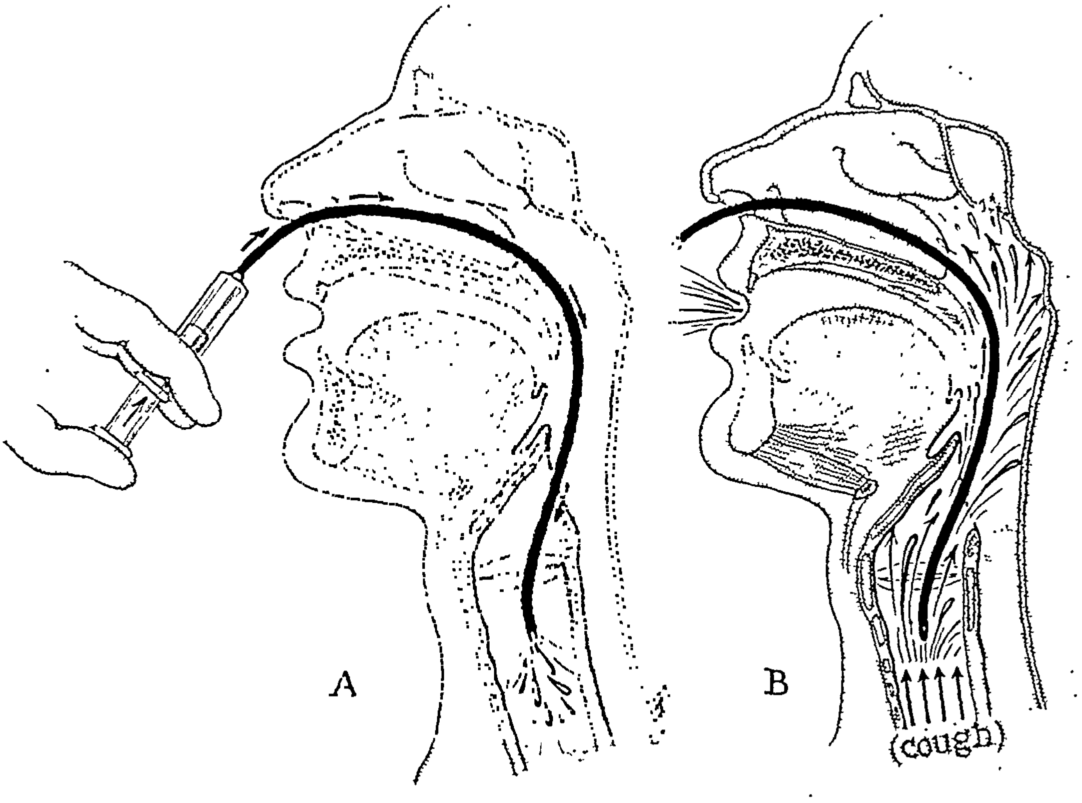

Fig. 1.—*A*, Nasotracheal instillation of cocaine. Note firm control of syringe barrel to prevent expulsion during coughing.
B, Dissemination of cocaine by coughing, with resultant oropharyngeal anesthesia.

DISCUSSION

The present method employs the same principle as transtracheal anesthesia[2] in which the topical agent is introduced into the trachea from where it is disseminated into both upper and lower air passages by respiration and coughing. Certain advantages are apparent in the present method, however, including the avoidance of needle puncture of the trachea, and the opportunity of making a slow injection of the drug.

The routine use of the described technique has considerably reduced the period of preparation for bronchoscopy or bronchography. In almost every instance the patient is ready for study within 5 or 10 minutes after arrival in the operating room.

A number of patients in this series had had previous bronchoscopy or bronchography after the induction of topical anesthesia by the usual means. Without exception, these patients have expressed a preference for the described method.

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POTASSIUM, MAGNESIUM, AND NEOSTIGMINE FOR CONTROLLED CARDIOPLEGIA

A Report of Its Use in 34 Patients

Will C. Sealy, M.D., W. Glenn Young, Jr., M.D., Ivan W. Brown, Jr., M.D., Jerome S. Harris, M.D., and Doris H. Merritt, M D., Durham, N. C.

In 1956 the first of a series of studies[1] was reported by the authors on the feasibility of using induced cardiac standstill as an adjunct to open-heart surgery. Subsequently, other experiments[2] were outlined using the isolated cat heart to monitor many different cardioplegic substances. These studies revealed that a solution of potassium citrate, magnesium sulfate, and neostigmine (Prostigmin) constituted the most efficient cardioplegic agent. This technique was then used successfully on the dog with the addition of extracorporeal circulation and hypothermia.[3] The favorable experimental results then permitted its trial on patients. This method of induced cardioplegia has now been used on 34 patients undergoing right ventricular exploration, and the experience with these patients is the subject of this final report.

METHODS

The cardioplegic solution contained potassium citrate, 0.81 per cent, and magnesium sulfate (hydrated), 2.46 per cent, made in distilled water which in turn made an isotonic solution. Just before use, 1 mg. of neostigmine per 100 c.c. was added.

The electrocardiogram was monitored throughout the immediate prewashout and post-washout periods and during the standstill. The time for complete standstill to occur after injection, the time of standstill, the time of occurrence of a strong rhythmical beat, and the return of sinus rhythm were all noted.

For injection of the cardioplegic solution, the ascending aorta was occluded above the coronary arteries. A curved No. 18 needle was placed in the aortic lumen, the aorta occluded, and then the solution forcibly injected into the coronary arteries. At the end of the intracardiac procedure, the occluded aorta was released, and the extracorporeal perfusion washed the cardioplegic compound from the heart.

From the Department of Surgery and Pediatrics, Duke University School of Medicine, Durham, N. C.

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Extracorporeal circulation was maintained by means of a *modified DeWall* oxygenator and a finger occlusive pump.[4] In the first 8 patients, however, plastic bags were used for oxygenation. In the initial 12 patients of the series, *external body cooling* was employed to induce the state of hypothermia, while in the remainder this was both induced and corrected by direct cooling and rewarming the blood with a Brown-Emmons heat exchanger[5] incorporated in extracorporeal system. Details of this technique have been described elsewhere.[6] Temperatures of from 28.5° to 30° C. were sought, and the rates of perfusion of 25 c.c. per kilogram in adults and 50 c.c. per kilogram in children were usually employed.

RESULTS

In the 34 cases, 3 were complicated neonatal lesions. The heart was successfully stopped and restarted in all, but the patients died either on the operating table or within the first few hours afterward.

In the remaining 31 cases, there were 22 patients who survived (Table I). In none of the fatalities was the induced cardiac standstill thought to be a major factor influencing the outcome. Four of the deaths occurred on the operating table. In all, the heart was successfully stopped and restarted, but death occurred in one because of an unrecognized aortic stenosis. In another, the aortic stenosis was produced by the closure of the ventricular defect in a patient with tetralogy of Fallot with a marked dextroposition of the aorta. The remaining patients had what was considered to be an irreversible pulmonary hypertension and resistance, and all had had episodes of congestive failure. With the exception of one patient who died from heart block 14 days after surgery, the remaining patients died in the first 36 hours after operation from factors related primarily to their disease.

TABLE I. SURVIVAL DATA ON 31 PATIENTS SUBMITTED TO RIGHT VENTRICULOTOMY AND CARDIOPLEGIA

DIAGNOSIS	NO. PATIENTS	NO. SURVIVED	NO. DIED	COMMENT
I.V. pulmonary pressure less than 80 per cent of aortic pressure	14	11	3	1 died in 12 days from heart block 2 patients over age 25 had recent congestive failure
I.V. pulmonary pressure 80 per cent or greater than aortic pressure	6	3	3	1 had associated aortic stenosis
Tetralogy of Fallot	11	8	3	2 patients over age 25 and 1 recent congestive failure 1 patient died because of obstruction to aorta

The efficiency of this solution in inducing cardioplegia is shown in Table II. In earlier patients, due to faulty injection technique, larger amounts of the cardioplegic solution were used than have been needed in later patients.

Standstill occurs promptly; and, when injected under adequate pressure, amounts of 30 c.c. to 50 c.c. are usually adequate. In 80 per cent of the instances, cardiac arrest occurred promptly, usually within the first 30 seconds. In the remaining 20 per cent, there was a delay of 60 to 120 seconds. This delay was very likely due to the lack of adequate pressure in perfusion of the coronary arteries.

TABLE II. CARDIOPLEGIC DATA ON 31 PATIENTS

AMT. KMP (C.C.)		TIME FOR ARREST (SEC.)		TIME FIRST BEAT (SEC.)		TIME REGULAR BEAT* (SEC.)		TIME SINUS RHYTHM* (MIN.)	
AVG.	LOW-HIGH	AVG.	LOW-HIGH	AVG.	LOW HIGH	AVG.	LOW HIGH	AVG.	LOW-HIGH
54	25-100	15	10-66	29	10-66	142	20-600	7	4-12

*21 patients whose hearts did not fibrillate.

Following standstill in 24 of the 34 patients, the heart action returned promptly, usually in 29 seconds. Ten of the patients developed ventricular fibrillation just after opening the coronary arteries. Nine of these 10 hearts were successfully defibrillated by electrical stimulation; while the tenth spontaneously resumed normal rhythm. Strong forceful beats developed on an average of 2½ minutes after washout; while normal sinus rhythm appeared in approximately 7 minutes. Post-washout arrhythmias other than fibrillation were not striking. One patient had a persistent heart block which caused the *patient's death 12 days after surgery. Perfusion rates, temperature, and* occlusion time in 31 patients are shown in Table III. Temperatures as low as 28.5° C. have not interfered with the correction of ventricular fibrillation when hypothermia was employed with the assistance of extracorporeal circulation.

TABLE III. PERFUSION DATA ON 31 PATIENTS SUBMITTED TO RIGHT VENTRICULOTOMY AND CARDIOPLEGIA

DIAGNOSIS	NO. PATIENTS	TEMPERATURE (° C.)		FLOW ML./KG./MIN. (ML.)		DURATION OF PERFUSION (MIN.)		DURATION CORONARY OCCLUSION (MIN.)	
		AVG.	LOW-HIGH	AVG.	LOW-HIGH	AVG.	LOW-HIGH	AVG.	LOW-HIGH
Ventricular septal defect	20	30.6	28-30	49	26-63	34	16-55	15	7-21
Tetralogy of Fallot	11	30	26-32	47	33-65	45	30-65	23	11-38

DISCUSSION

The surgical advantages of induced cardiac standstill are obvious and have been discussed in previous papers. Whether or not these benefits outweigh the disadvantages of prolonged ischemia and possible local toxic action of the solution is still not proved. Laboratory studies by the authors on the dog indicate that it will safely permit 45 minutes to an hour of coronary occlusion when the heart is cold. The clinical experience reported here is interpreted as confirming our laboratory finding. The recent report of Sloan and colleagues,[7] using only potassium and magnesium for cardioplegia at normal body temperatures, is further evidence of the safety of this method.

A combination of potassium citrate, magnesium sulfate, and Prostigmin together appeared to be a more satisfactory cardioplegic when tested in the laboratory than potassium citrate used alone. Acetylcholine is not considered a cardioplegic. The use of two cardioplegics with different modes of action was sought both for possible synergistic action and reduction of the concentration of both electrolytes needed for effective action. The potassium ion most likely acts at the cell membranes, blocking the polarization of the cell, while the magnesium ion probably inhibits the energy transfer mechanism in the heart muscle. Prostigmin was added because of its vagotonic effect which would tend to prevent fibrillation during hypothermia and allow a slow heart rate in the immediate post-washout period.

When this work was first begun, it was postulated that the major problem to be solved was the control of ventricular fibrillation in the cold heart. As has been pointed out in previous papers, this was one of the reasons for searching for a method of cardioplegia. These fears have proved unfounded, for in no instance has it been difficult to defibrillate a heart when using hypothermia combined with extracorporeal circulation. This problem is not comparable to the irreversible ventricular fibrillation that may develop in patients with hypothermia and complete circulatory standstill. In fact, the hypothermia is considered to be beneficial, for experimental evidence, already reported from this laboratory as well as studies of Gollan,[8] suggests strongly that the cold nonbeating ischemic heart remains in a better functional state than does the warm nonbeating ischemic heart.

A combination of hypothermia and extracorporeal circulation has other important effects that have to be considered in the interpretation of the results of this cardioplegic technique. Even the nonworking heart, after a long period of ischemia, may not recover completely if the metabolic state of the remainder of the body is poor. The heart then may not be able to compensate for its own debt and that accumulated by the whole organism. In this regard, it is of interest that others have reported, during hypothermia, serious rhythm disturbances following vena caval occlusion even though perfusion was maintained in the coronary system.[9] One of the requisites for use of cardioplegia is an adequate system of maintaining good oxygenation of the entire body.

Certain technical problems encountered in using this technique warrant emphasis. It is imperative that the cardioplegic solution be injected in the coronary arteries with enough pressure to cause closure of the aortic valve. If this is not done, poor perfusion occurs and the heart may not be brought into complete standstill. The problem of distention of the left side of the heart after closure of the shunt has not been a problem with the patients outlined here because of the reduced flow rates employed, although this is an important consideration. It is of utmost importance to assist the circulation by continued perfusion after the period of cardioplegia. Because of the necessity of this, the technique is now employed of placing one venous catheter in the femoral vein and the arterial catheter in the femoral artery so that perfusion can be continued for as long as desired after the washout. It is not unreasonable to expect a metabolic deficit of the heart to be such that several minutes are required before it returns to a relatively normal state.

CONCLUSION

A combination of potassium, magnesium, and Prostigmin has by clinical trial proved to be an effective and safe cardioplegic technique when used in combination with hypothermia and extracorporeal circulation.

ADDENDUM

Since preparation of this manuscript, 10 additional patients with either tetralogy of Fallot or interventricular septal defects have been operated upon, using the above techniques for cardiac standstill. There were no deaths.

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OBTURATORS FOR EXTRACORPOREAL CIRCULATION CANNULAE

Edward A. Fitch, M.D., and Charles P. Bailey, M.D.,** Philadelphia, Pa.*

Many types of heart-lung machines are currently in clinical and experimental use. There is an almost innumerable number of combinations of these machines with the various techniques and accessories of which they are the integral part. Complete and partial circulatory bypass of the heart and lungs, right or left heart bypass, autogenous lung preparations, segmental aortic bypass, and organ and partial body perfusion are a few of the basic circulatory schema that have been devised. When filters, depulsators, flow meters, etc., are incorporated into the circuit, the possibilities become complex indeed.

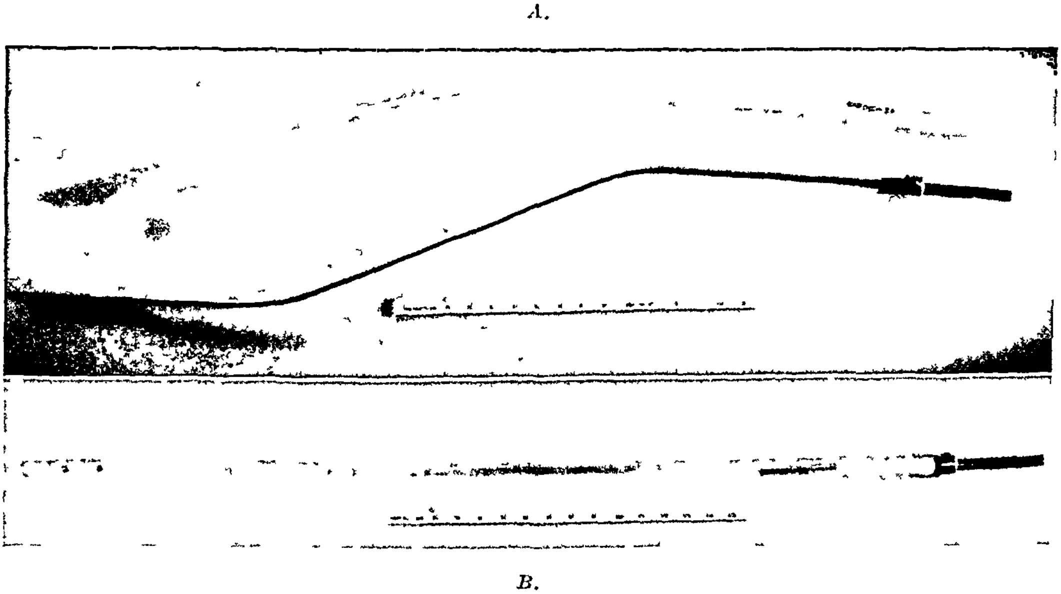

Fig 1.—*A* and *B*. The smaller obturators clip onto the catheter's adapter and occlude the distal perforations to prevent blood loss

The problem of cannulation, however, is one item that is common to all systems. Even here, dozens of techniques involve cannulation of various vascular structures and cardiac chambers. Many types of tubing are suitable for

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*Resident in Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pa. Public Health Service Research Fellow of the National Heart Institute.

**Professor and Head of the Department of Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pa cannulation purposes, but perhaps the one in most widespread use in this country is the Bardic catheter.* Early in our experience with extracorporeal circuits, it became obvious that some mechanical aid in the introduction of the cannulae was desirable This is particularly true in four instances

First, a common problem is the encountering of obstructing trabeculae in the right atrium and the atrial appendages Second, the accurate placement of catheters in a site remote from the point of introduction is often frustrating, such as the cannulation of the venae cavae or the coronary sinus after penetration of the atrial wall. Third, cannulation of a vascular chamber deep in the depths of the wound must be done "at a distance," and this is often difficult

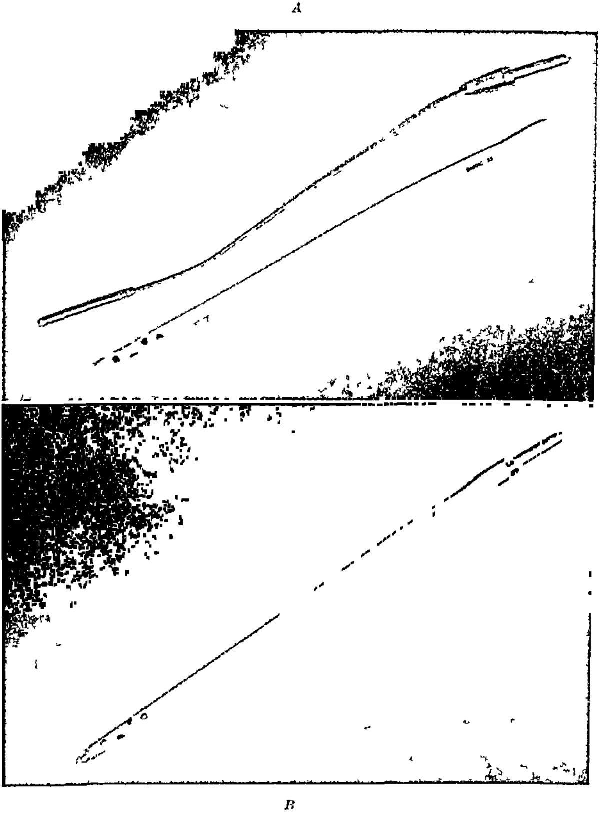

Fig 2—*A* and *B*, Larger sizes incorporate a shoulder to occlude the flared proximal end of the catheter A distal plug is added to occlude the perforations

with a flaccid catheter. Last, due to the multiple perforated nature of the catheter tip, blood loss is frequently encountered during introduction by the passage of blood from an intravascular perforation to an extravascular one.

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*C R. Bard Co, Summit, N J

An instrument* was devised by one of us (E. A. F.) to overcome all of the above-mentioned problems. This obturator was made specifically for use with the stock models of Bardic catheters. Its design varies slightly with the different sizes of catheters. The two common features of all the obturators are an annealed copper shaft and a suitable handle. In the smaller sizes (10 Fr. through 20 Fr.), the copper shaft itself provides the occluding mechanism for the multiple perforations. A clip mechanism fixes the adapter snug against the butt plate of the handle, preventing slipping of the catheter on the shaft, and further blocking any blood which may escape to the end of the catheter.

As the sizes of the catheters increase (22 Fr. through 40 Fr.), a length of stainless steel plug is added on the end of the copper shaft to occlude the distal perforations. The end of the obturator extends slightly beyond the distal end of the catheter. This rounded point provides for easier introduction of the larger sizes.

The larger sized catheters (30 Fr. through 40 Fr.) are not equipped with commercially attached adapters. Rather, the proximal end is slightly flared. An adaptation of the proximal end of the obturator consisting of a rounded shoulder to plug the flared end of the catheter is provided. This fits snugly into the catheter and serves the same purpose as the clip on the smaller obturators.

The handle of each obturator is stamped with the size of the catheter for which it is designed. A bit of water soluble lubricant or mineral oil applied to the shaft allows easy withdrawal of the obturator. The instrument transforms a flexible, collapsible, kinking catheter into a semi-rigid shaft for leisurely cannulation.

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*Obtainable from G. P. Pilling & Sons Co., Philadelphia, Pa.

THE RELATIONSHIP BETWEEN PERFUSION BLOOD TEMPERATURE AND AVAILABLE VENOUS RETURN DURING EXTRACORPOREAL CIRCULATION

Evan F Lindberg, M D , Augusta, Ga*

SEVERAL types of mechanical circulation pump oxygenators have been developed which allow the successful bypass of the heart and lungs in both dog and man The changes in hematological and biochemical normality of the blood, produced by the pump, have been studied repeatedly[1-3] The physiologic importance of some of these changes still remains unexplained Since Andreason[4] first described the survival of dogs after the total flow was restricted to that from the azygos vein for 30 minute periods, investigators have tried to determine whether a low flow rate or a rate of flow near normal would produce the best results for the surgeon Those who prefer to work with the "high" flows discovered that with the institution of the bypass, the venous return fell sharply and the pump output was consequently below that of the resting cardiac output Most of the groups have employed transfusions of what appear to be large quantities of blood to ensure an adequate pumping rate Recently some investigators have turned their attention to the factors which control the rate of venous return,[5,6] since this has been the major limitation on the arterial output from the pump

The origin of this fall in venous return may lie in the size of the cannulae which have been used for caval drainage, or it may reflect a peripheral pooling of blood perhaps related to the increased resistance of this tubing It has been demonstrated that a moderate increase in central venous pressure, produced by a small increase in resistance, resulted in a serious curtailment of venous return and an irreversible shock state[7]

At the start of the present bypass experiments, this decrease in venous return was always present Further, in many cases, the expansion of the circulating blood volume by arterial transfusion resulted only in a temporary increase in venous return An incidental observation made was that those animals who were most refractory to the transfusions were those which showed an appreciable drop in rectal temperature While this might be attributed to

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From the Dept. of Physiology Medical College of Georgia Augusta Ga

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*Present Address Aeromedical Laboratory Wright Patterson AFB Dayton Ohio a low rate of peripheral blood flow, it called to mind the experiments of Gollan, Blos, and Schuman[8] which demonstrated a clear parallel between body temperature and the rate of venous return to the heart.

Therefore, three types of experiments were conducted.

GROUP A: To find whether the failure of venous return was due to loss of plasma or blood from the circulation, we measured the dog's blood volume (using T-1824 dye) before and after the institution of the extracorporeal circulation.

GROUP B: To observe the venous return at different perfusing blood temperatures, the bypass was instituted and the rate of venous return recorded as the perfusing blood temperature was altered.

GROUP C: To test the ability of blood transfusions to increase the rate of venous return, known quantities of blood were transfused with the perfusing blood temperature held at different levels.

METHODS

Mongrel dogs, weighing 11 to 21 Kg., were premedicated with morphine (10 mg./Kg.) and anesthetized with sodium pentobarbital (20 mg./Kg.). A No. 20 Fr. catheter, which was to receive the pump outflow during perfusion, was passed into the proximal end of the left common carotid artery. The control studies, listed in detail below, were made and the chest was entered through a right fourth intercostal space incision. Respiration was maintained with intermittent positive pressure. Loose ligatures were placed around the superior and inferior venae cavae. The animal was given 3 mg. per kilogram of body weight of heparin. The inferior vena cava was cannulated with a No. 26 Fr. catheter through the right atrial appendage, so that the catheter tip lay 2 to 3 cm. above the diaphragm. A No. 24 catheter was placed 3 to 4 cm. into the superior vena cava through a stab incision in the right atrial wall and secured with a purse-string suture. The pump tubing was filled with 1,100 c.c. of heparinized donor blood collected from unanesthetized dogs, and connections were made with the recipient's cannulae. A Model T-69 Sigmamotor pump was used for these experiments. All measured blood loss from surgery and sampling was replaced prior to starting the perfusion. As the bypass began, the caval ligatures were tightened around the cannulae so that all caval and azygos blood entered an already established siphon column into the venous pump reservoir. The level of this siphon reservoir kept the venae cavae flaccid but not collapsed. The caval cannulae were adequate to siphon three to four times the flows encountered in these experiments. From the siphon reservoir the blood was pumped into a DeWall bubble-type oxygenator system.[9] With the venous pump running at a rate exceeding venous return and the inflow tube to the venous pump placed above the end of the siphon column (Fig. 1), the siphon was maintained by a constant level of blood in the reservoir. From the oxygenator and defoaming chamber, the blood flowed into a calibrated helix reservoir. Thus, the exact amount of extracorporeal blood could be calculated at any given moment Radiant heat lamps were used to warm the blood as it flowed through the helix The blood was then pumped into the carotid artery cannula, thus completing the bypass of the recipient's heart and lungs The flow values during perfusion were taken from the vernier scale on the arterial pump This pump was calibrated repeatedly, and outputs found to be consistent at the pressures present in these experiments A 2 to 5 minute period of adjustment of the arterial pump output to equal the venous return was necessary so that a constant level could be maintained in the reservoir and the venous return would be equal to the rate of flow from the pump

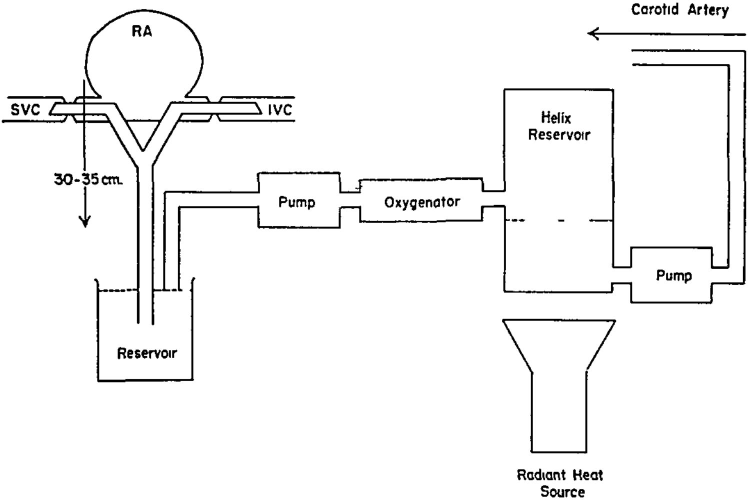

Fig 1

This obviated any change in the animal's blood volume due to addition or subtraction of blood by the pump The studies during perfusion were then performed for comparison with the control period, and, upon their completion, the animals were sacrificed Two successful survival experiments were performed as a clinical test of the equipment After each experiment, all tubing and fittings which were in contact with the blood were cleaned with Haemosol and soaked in a solution of Zephiran before reassembly

In all the experiments, a continuous record of rectal temperature was taken on a Weksler recording thermometer

Splenectomy was acutely performed on all dogs in the Group A and the Group C experiments, where an attempt was made to do blood bookkeeping In the former, small polyethylene cannulae were passed through the right femoral artery and vein into the abdominal aorta and inferior vena cava to a level above the renal vessels Pressures measured through these cannulae by

Statham strain gauges were recorded on the Sanborn Twin-Viso. Zero reference level for all pressures was that of the right atrium. Two small cannulae were also placed into the superior vena cava via the jugular vein; one was used for the dye injections while the other acted as a convenient site for sampling of superior vena cava blood. To measure the control cardiac output, a slug injection of T-1824 dye was made into the superior cava and arterial samples were collected during the initial circulation of this dye. The dye concentrations in plasma from these samples were determined on a spectrophotometer and the control cardiac output calculated using the method of Hamilton and associates.[10] Samples were taken from the three polyethylene cannulae for hematocrit and plasma specific gravity determinations both during control and perfusion periods. The gravity studies were made using the falling drop technique of Barbour and Hamilton.[11] The blood for the hematocrits was placed in Wintrobe tubes and spun at 3,000 r.p.m. for 30 minutes. These values were also obtained for the donor blood so that the expected changes could be calculated when the extracorporeal blood was added to the circulation. Plasma volume was measured by dividing the known amount of T-1824 blue dye injected by the average concentration in plasma samples withdrawn at intervals of 10, 20, and 30 minutes. Processing of these samples has been described by Dow and Pickering.[12] The blood volume was then calculated by dividing the plasma volume by 1 minus hematocrit value. On the assumption that only the "central" blood volume would be increased by the quantity of blood in the extracorporeal circuit, no F-cell correction of the initial hematocrit reading was made.[13] When the maximal rate of perfusion had been established in the manner described above, the blood volume, plasma specific gravity, and hematocrit determinations were repeated. In order to measure the animal's blood volume during bypass, it was necessary to subtract the quantity of blood in the extracorporeal unit from the amount measured by the dye. Total peripheral resistance values were calculated by dividing the mean arterial pressure by the flow in cubic centimeters per kilogram per minute, as measured either by the dye injection method during the control period or by the arterial pump output during perfusion.

In the Group B experiments the arterial and venous pressures were recorded by Hamilton optical manometers. Instead of a polyethylene cannula, a long metal sound was passed up the aorta from the femoral artery to the aortic arch and central pressure pulses obtained. The cardiac outputs were calculated from these tracings using the method described by Remington.[14] Following the caval cannulations the bypass was instituted in the same manner as in the Group A experiments. The perfusing blood was then warmed by the heat lamps or cooled by perfusing without any external source of heat, and the changes in flow rate, as determined by the venous return, were recorded. The perfusing blood temperature ranged from 94° to 106° F. As in the previous group of experiments, no change in the animal's blood volume was effected by the pump itself.

TABLE I. RESULTS FROM 4 DOGS IN THE GROUP A EXPERIMENT

EXPER. NO.	MEAN ARTERIAL PRESSURE (MM. HG)		INFERIOR CAVA PRESSURE (MM. HG)		BLOOD FLOW (C.C./KG./MIN.)		T. P. R.* (MM. HG) (C.C./KG./MIN.)		BLOOD VOLUME (C.C./KG.)		CHANGE IN RECTAL TEMP. (DEGREES F.)
	CONT.	PERF.	CONT.	PERF.	CONT.	PERF.	CONT.	PERF.	CONT.	PERF.	
17	140	100	+5	+1	96	57	1.45	1.75	112	110	-1
18	160	160	+2	-1	150	95	1.06	1.70	112	100	-1
19	140	100	+3	-2	99	33	1.40	3.00	81	101	-6
21	130	110	-	-	115	57	1.10	1.90	116	137	-2
Average	143	118	+3	-1	115	61	1.25	2.09	105	112	-
Per cent of control		83%				53%		167%		107%	

*Total peripheral resistance.

Hemodynamic changes as the result of the institution of a cardiopulmonary bypass on 4 dogs (Group A experiment).

TABLE II. ABSENCE OF CHANGE IN BLOOD VOLUME AS DEDUCED FROM HEMATOCRIT AND PLASMA SPECIFIC GRAVITY VALUES DURING A BYPASS

EXPER. NO.	RECIPIENT			1100 C.C. PUMP BLOOD		EXPECTED VALUES AT EQUILIBRIUM		MEASURED VALUES	
	BLOOD VOL. (C.C.)	PLASMA (SP. GR.)	HCT. (%)	PLASMA (SP. GR.)	HCT. (%)	PLASMA (SP. GR.)	HCT. (%)	PLASMA (SP. GR.)	HCT. (%)
17	2,150	1.0249	47	1.0233	30	1.0241	41	1.0239	39
18	2,500	1.0245	33	1.0271	51	1.0253	39	1.0253	41
19	1,720	1.0263	52	1.0250	43	1.0260	48	1.0259	48
21	1,850	1.0250	49	1.0251	48	1.0250	49	1.0250	48

The results from four Group B experiments are shown in Table III. Once again the perfusion values are related to the control period values. The rectal temperature was usually 1° F less than that of the perfusing blood and followed the changes in the blood temperature closely. During perfusion, when the blood temperature was raised, an increase in venous return followed; when the blood temperature was lowered the rate of venous return decreased. It should be emphasized that the pump output was altered to match these changes in venous return and thereby prevent a change in the animal's blood volume. Depending upon the amount of blood in the circuit, a 5 to 15 minute period was required to effect these changes in blood temperature. In those experiments in which the blood temperature was raised, the flow increased to a degree greater than the increase in arterial pressure so that a decrease in total peripheral resistance resulted. The arterial pressure fell less than the flow decreased in those experiments in which the perfusion blood temperature was dropped and, thus, an increase in total peripheral resistance was the result. Experiment 4 began with a high blood temperature which was increased even more and the increase in venous return still occurred.

Table IV lists the results of the Group C experiments in which the effect of a transfusion upon the rate of venous return was studied in animals having different perfusing blood (and rectal) temperatures. In Experiment 25 the institution of the bypass caused a decrease in flow (or rate of venous return) from 135 to 44 c.c./Kg./min. (Columns 1 and 3). A transfusion of 32 c.c./Kg. of blood (Column 5) was then made from the helix reservoir. There was an immediate transient rise in venous return but by the end of 3 minutes the flow rate had returned to 46 c.c./Kg./min. (Column 6), a value essentially the same as before the transfusion. That the amount of blood transfused was still present in the circulating volume was shown by the increase in blood volume as measured by dye. Hence the sum of the initial blood volume (Column 4) and the transfusion volume (Column 5) was 121 c.c./Kg. as compared with the measured total volume of 124 c.c./Kg. (Column 7). Experiment 26 duplicated the last except that the perfusing blood temperature was 102° F instead of 95° F. Once again there was a drop in flow rate as perfusion began. The effect of the transfusion of 76 c.c./Kg. on the venous return was immediate and, with this warm blood, the flow rate was maintained above control levels. Once again the change in circulating volume was quantitatively shown by the dye volume measurement (Columns 9, 10, and 12). The last two experiments further demonstrated that the temperature of the perfusing blood was very important if an increase in flow rate was to be maintained by transfusion. In Experiments 26 and 29, the transfusion into hot recipients raised the flows to the range of the control cardiac outputs. When this was achieved, the total peripheral resistance figures were also close to the control values.

DISCUSSION

The results of these experiments eliminated some of the possible explanations for the decreased rate of venous return to the extracorporeal circulation

TABLE III. THE EFFECTS OF PERFUSION BLOOD TEMPERATURE ON VENOUS RETURN (BLOOD VOLUME KEPT CONSTANT)

EXPER. NO.	MEAN ARTERIAL PRESSURE (MM. HG)		TOTAL BLOOD FLOW (C.C./KG./MIN.)		T. P. R. (MM. HG) (C.C./KG./MIN.)		RECTAL TEMPERATURE (DEGREES F.)		PERFUSION BLOOD TEMPERATURE (DEGREES F.)
	CONTROL	BYPASS	CONTROL	BYPASS	CONTROL	BYPASS	CONTROL	BYPASS	
22	124	112 130	130	48 87	0.7	2.3 1.5	97.5	95.0 98.0	94 100
23	115	105 90	145	79 40	0.8	1.45 2.24	97.5	98.0 96.0	100 96
24	120	105 110	140	24 43	0.85	4.30 2.6	99.0	97.5 100.0	96 102
28	121	108 135	160	70 75	0.8	1.55 1.65	101.0	103.0 105.0	104 106

TABLE IV. THE EFFECT OF BLOOD TRANSFUSION ON THE FLOW RATE WHEN THE PERFUSING BLOOD TEMPERATURE WAS ALTERED

EXPER. NO.	CONTROL PERIOD		PERFUSION PERIOD									
			BLOOD TEMPERATURE 95° F.					BLOOD TEMPERATURE 102° F.				
	FLOW*	BLOOD VOL.†	FLOW*	BLOOD VOL.†	TRANS. VOL.†	FLOW*	BLOOD VOL.†	FLOW*	BLOOD VOL.†	TRANS. VOL.†	FLOW*	BLOOD VOL.†
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
25	135	89	44	89	32	46	124					
26								56	82	76	161	145
27	145		46		15	50		60		38	93	
29	180		85		34	90		95		85	186	

*Flow values are in c.c./Kg./min.

†Blood volume and transfusion volume are recorded in c.c./Kg.

It was apparent that mechanical blockage of the venous return by the drainage cannulae was not a problem since the pressures recorded in the upper abdominal vena cava were either low or negative. In addition, it was possible to increase the rate of venous return by raising the temperature of the perfusing blood.

Thus, it was evident that, with the institution of the bypass circuit, the amount of blood available to the caval cannulae decreased almost immediately. There was an associated increase in total peripheral resistance, since the arterial pressure was maintained in the presence of a failing venous return, and, hence, a decreased arterial pump output. Since the T-1824 dye concentrations in samples taken from the three sites were essentially the same (indicating good mixing), this increase in peripheral resistance was thought to be a generalized phenomenon and not the result of the elimination of one vascular bed or another from the circulation. The amount of circulating blood and plasma was the same during perfusion as in the control period, as shown by the dye volume, plasma gravity, and hematocrit studies.

To understand a decrease in venous return in the presence of a normal circulating blood volume and an unimpeded venous drainage, it is necessary to propose the presence of an intravascular pool of blood somewhere retrograde to the large veins. In the presence of an elevated perfusing blood temperature, the venous return to the pump increased. It appeared that the ease with which blood was mobilized from this pool, and presumedly its size, was a function of the perfusing blood temperature. This conclusion was further substantiated when the effect of expanding the recipient's blood volume on venous return was studied. Those animals perfused with cool blood demonstrated the ability to expand their circulating blood volume with transfusion without an appreciable increase in venous return. On the other hand, the increase in venous return following transfusion was readily apparent in those animals perfused with the warm blood. The change in peripheral capacity with temperature is, of course, quite opposite to that one might anticipate, and provides a provocative question as to just where the anatomic site of this variable peripheral blood pool might be.

SUMMARY

No significant changes in blood volume, plasma specific gravity, and hematocrit values were found in dogs before and after the institution of a heart-lung bypass pump-oxygenator. The formation of an intravascular pool of blood, in the presence of an increased total peripheral resistance, is proposed as a possible explanation for the decrease in venous return when the extracorporeal circulation was started. The effect of alterations in the perfusing blood temperature on venous return was studied. The rate of venous return was found to parallel the rise or fall in perfusing blood temperature. Expansion of the circulating blood volume of the recipient animal was found to be effective in increasing the venous return only if the perfusing blood temperature was high.

The author wishes to gratefully acknowledge the technical and conceptual help given him by John W. Remington, Walter J. Brown, Jr., and Charles R. Wallace.

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GRADUAL CLOSURE OF INTERVENTRICULAR SEPTAL DEFECTS

Riccardo Benvenuto, M.D., and F. John Lewis, M D., Chicago, Ill.

INTRODUCTION

The abrupt closure of an interventricular septal defect in patients with high pulmonary pressure may result in death due to several causes, in part not entirely known. Because of this high risk, patients with high pulmonary pressure, and particularly those with reverse shunt, have been considered inoperable.[2] Yet, if the hemodynamic changes induced by the operation could be more gradual or partial, the patients could survive the closure of the defect. Therefore, possible irreversible pulmonary vascular changes might be expected to become, in time, partially or completely reversible.

To achieve this result a technique to gradually close the defect by means of a perforated plastic plug has been devised. This is similar to the technique we have used previously for the slow closure of interatrial septal defects.[1] The results obtained experimentally in dogs are reported in the present paper.

METHODS AND MATERIALS

Thirty-nine healthy mongrel dogs, weighing between 24 and 49 pounds, were used. In all the animals, an interventricular septal defect was created and simultaneously closed by the insertion of different models of plastic plugs. These plugs were modifications of the Ivalon plug we previously used for one-stage repair of such defects.[3] All the plugs used had in common a central opening so as to allow the persistence of a shunt after their insertion. Final occlusion of this channel could be expected in time because of fibrin deposition and endothelial invasion.

Three different kinds of plugs were used. In 17 animals, the plug was made of compressed Ivalon sponge with an internal lining of Lucite (Fig. 1, *A*). This was obtained by imbedding a short piece of Lucite tube (3 mm. in length) within the Ivalon sponge. The internal diameter of the tube was 4 mm.

In a second group of dogs (7 animals), the plug used was made of compressed Ivalon sponge reinforced with an external ring of Teflon (Fig. 1, *B*).

From the Department of Surgery, Northwestern University Medical School, 303 East Chicago Ave., Chicago 11, Ill.

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Such a ring was limited to the central portion of the plug to provide a rigid support in the central portion of the channel without diminishing the flexibility of the device. Such a plug had an internal diameter of 6 mm.

The third type of plug (used in 15 animals) was similar to the one used in the second group of dogs but with an internal diameter reduced to 3 mm. Furthermore, the external ring of Teflon was thinner and perforated (Fig. 1, *C*).

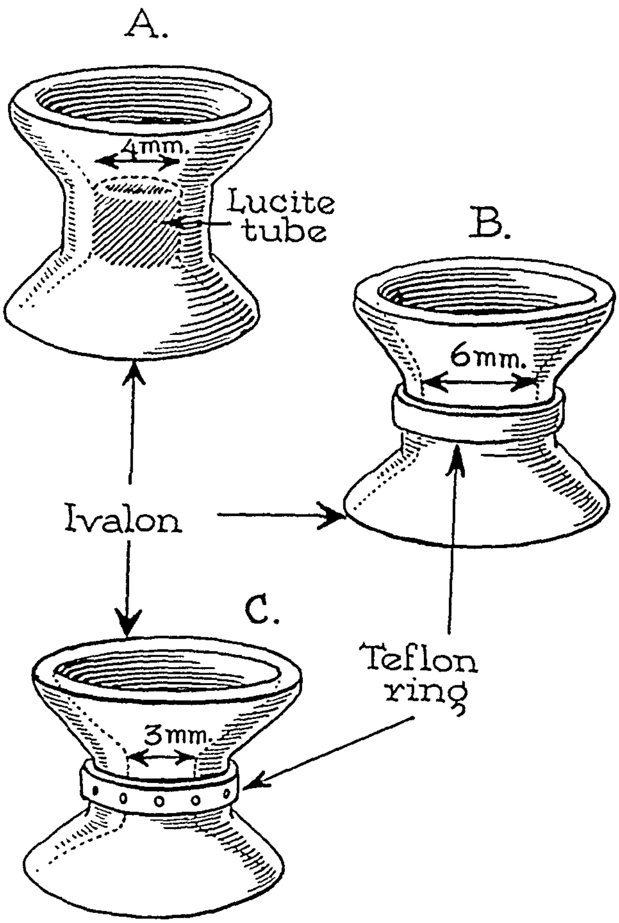

Fig. 1.—The three different models of Ivalon sponge plug used to repair interventricular septal defects.

The animals were operated upon during hypothermia using a respirator with a mixture of 95 per cent oxygen and 5 per cent carbon dioxide. A thoracotomy was performed in the right fourth intercostal space. With the usual technique employed for the open cardiotomies, the blood inflow to the heart was arrested and a right atriotomy was performed. The right ventricle was then entered through the tricuspid valve (Fig. 2). The defect was made in the high portion of the septum, trying to avoid the bundle of His. A cruciate incision was made in the septum and then the hole was enlarged with a right angle hemostat used in such a way as to provide simultaneous retraction. Bright red blood coming from the left ventricle was always noted at this point. After the introduction of the plug, the left ventricle was filled with saline, using a syringe and needle, and the right ventricle filled with blood by releasing the venae cavae.

Whenever the defect was successfully created, a clear systolic thrill was felt over the right ventricle. In the same way, a loud systolic murmur was heard over the precordium when the chest was closed (Fig. 3). This murmur was used as a guide to follow the gradual closure of the defect. When the murmur disappeared the animals were sacrificed and a postmortem examination was carried out

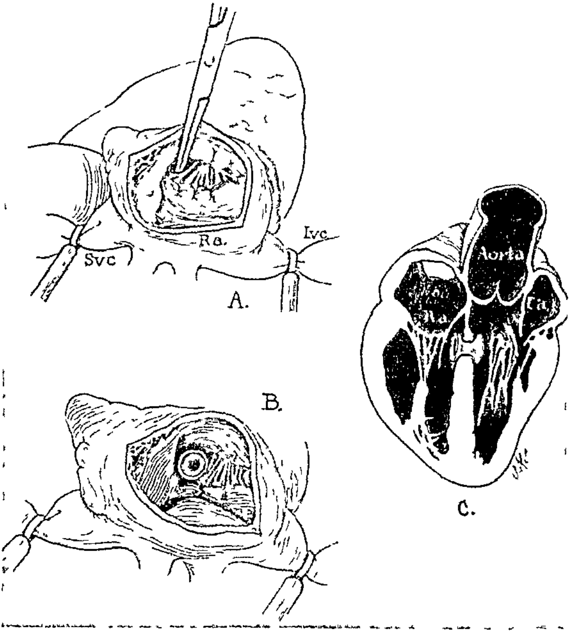

Fig 2—Technique for creation and repair of interventricular septal defects with a perforated Ivalon plug

A, The right ventricle is entered through the right atrium The septal leaflet of the tricuspid valve is retracted

B and *C*, The plug is inserted in position

Patency of the defect was studied intra-vitam by means of dye injection techniques. Evans blue was injected into the left ventricle by a direct percutaneous puncture and blood was simultaneously drawn from a catheter placed in the right ventricle. Detection of the dye in the blood obtained from the right ventricle was considered proof of the patency of the defect. In one instance a dye curve was recorded by means of a cuvette oximeter (Fig. 4).

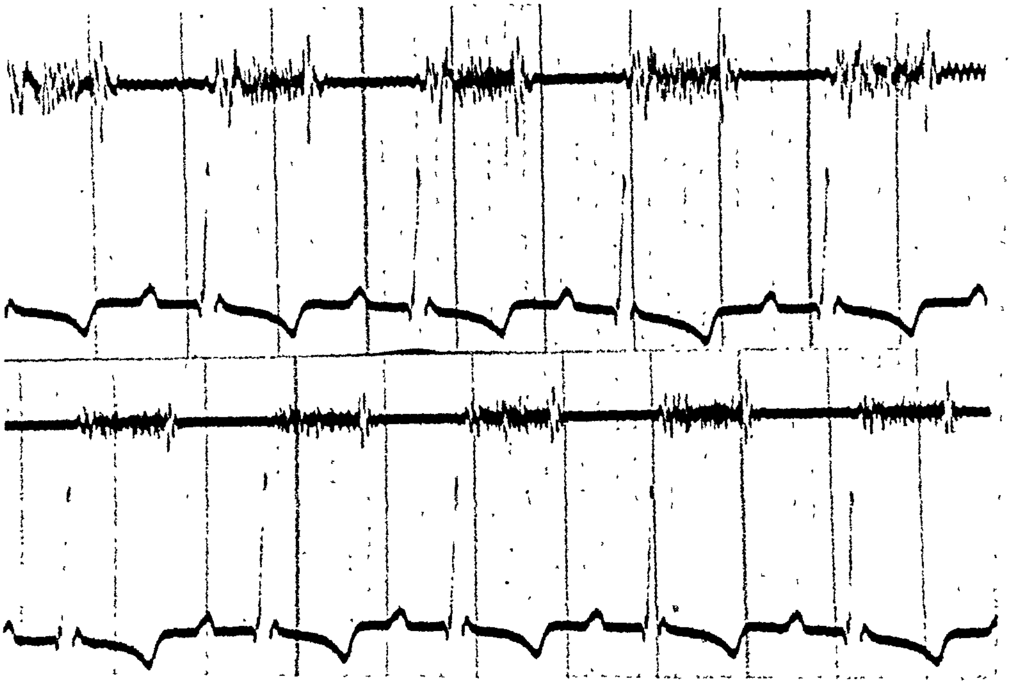

Fig. 3.—Phonocardiogram of Dog No. 489 showing a systolic murmur.

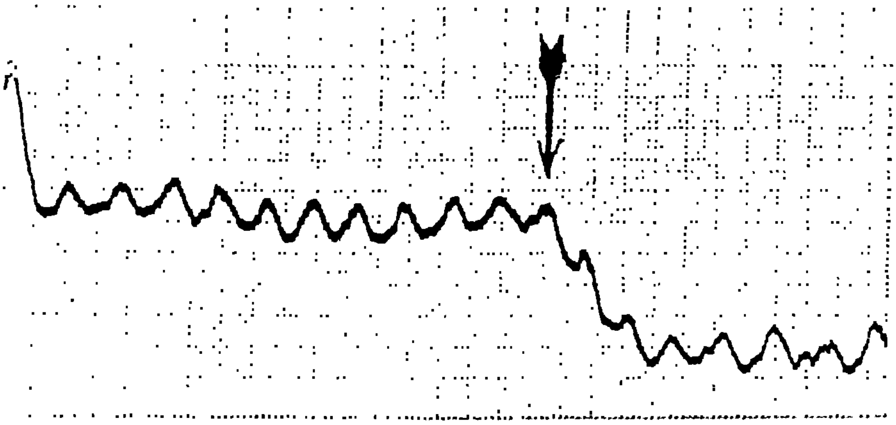

Fig. 4.—Dye curve recorded from Dog No. 477. Evans blue was injected into the left ventricle and blood collected from the right ventricle.

RESULTS

We found that when a plug with an internal lining of Lucite was used the defect closed too early. Thus, the closure of the defect was observed over a period of time ranging from 24 hours to 6 days. Table I shows the results obtained with this type of plug.

The second type of plug with an internal diameter of 6 mm. and an external ring of Teflon also proved to be unsatisfactory because of the development of acute heart failure. In fact, in 5 of the 6 dogs in which the plug was successfully inserted, an acute dilatation of the right ventricle occurred when the circulation was restarted This dilatation, in turn, started an irreversible ventricular fibrillation Table I summarizes the results obtained in this group of animals.

With the third type of plug we achieved our purpose The plug was inserted successfully in 10 animals and closure of the defect occurred in a period of time ranging from 4 to 41 days with an average of 26 days Autopsy revealed in all cases a plug well covered by surrounding tissue (Fig. 5). Table I shows the results obtained in this group of animals

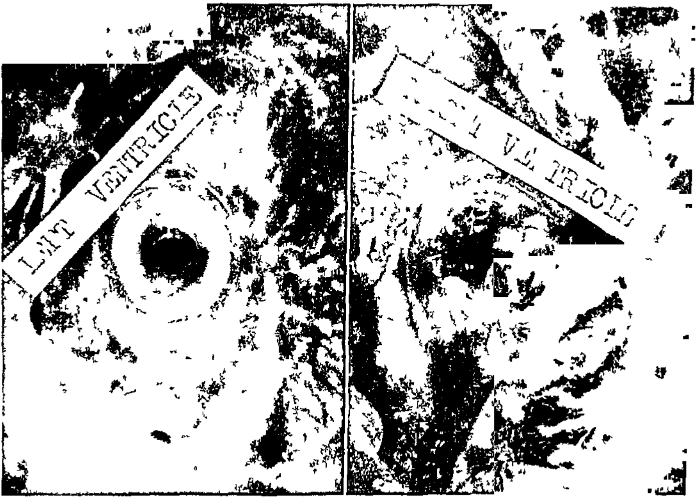

Fig 5 —Internal view of the right and left ventricles of a dog heart with the plug in place and covered by the surrounding tissue The dog was sacrificed when the systolic murmur disappeared 32 days after creation of the defect (Dog No 473—Plug C)

Table I. Results in 3 Experiments

RESULTS	PLUG A	PLUG B	PLUG C
Deaths	6	5	5
Plug improperly inserted	2	1	-
Satisfactory experiments	9	1	10
Total dogs operated upon	17	7	15

DISCUSSION

The early closure of the defect obtained in the first group of animals can be partially attributed to the limited lumen of the plug. Therefore, in the second model of the device the lumen was increased from 4 to 6 mm. The internal lining of Lucite was abandoned because it made the plug difficult to handle because of its rigidity

The acute dilatation of the right ventricle with subsequent irreversible ventricular fibrillation encountered when the second plug was used, can be attributed to the large shunt resulting in an acute overloading of the right ventricle. The reduction of the lumen of the device (Plug C) was adequate to overcome this problem and yet allow a sufficient length of time before occlusion.

In conclusion, a device capable of giving gradual closure of experimental interventricular septal defects has been successfully tested in dogs. Whether this achievement can be directly applied to human cases is difficult to say at present. The difference in pressure gradients can account for different behavior of a plug inserted in a human interventricular septal defect.

Perhaps the use of plugs with large holes in patients might be better tolerated since the heart, in such a case, is already hemodynamically accustomed to a large shunt. By using a larger hole one could probably expect a longer period of time before the complete occlusion of the plug, and, therefore, a more complete readjustment of the pulmonary circulation.

SUMMARY

1. Ventricular septal defects were created in dogs and simultaneously repaired by different models of plastic plugs.

2. All the plugs used had a central opening so as to allow the persistence of a shunt. This opening should occlude in time due to deposition of fibrin and endothelial invasion.

3. The best results were obtained with a plug having an opening of 3 mm. in diameter. Occlusion occurred in a period of time averaging 26 days.

4. The applicability of this method to human cases is discussed.

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PULMONIC STENOSIS DUE TO COMPRESSION OF THE PULMONARY ARTERY BY AN INTRAPERICARDIAL TUMOR

John A Waldhausen, M D, Carlos R Lombardo M D, and
Andrew G Morrow, M D, Bethesda Md

ALTHOUGH a significant percentage of mediastinal tumors arise within the pericardial space, only rarely does their presence cause impairment of cardiac function When this does occur it is usually attributable to impaired diastolic filling resulting from generalized compression of the heart by the infiltrated pericardium or from cardiac tamponade due to fluid accumulation Only rarely has obstruction to right ventricular outflow been described in association with an intrapericardial mass We have recently had opportunity to study and operate upon a patient in whom significant pulmonary stenosis resulted from compression of the main pulmonary artery by a primary malignant tumor

CASE REPORT

J A C, a 23 year old white man, had been in good health until January, 1958, when he developed pain in his throat and was treated by his physician for tonsillitis and streptococcal pharyngitis Shortly thereafter, he noted pain in his chest which fluctuated in intensity and was accentuated by deep breathing, coughing, and changes in position He was hospitalized at this time and, on physical examination, the pharynx was noted to be mildly injected and there were palpable nodes in the left anterior cervical triangle The pulse rate was 100, the heart was not enlarged and there was no precordial murmur However, an electrocardiogram revealed changes typical of pericarditis and the patient was noted to have daily temperature elevations to 100 5° F

Two weeks after admission, a pericardial friction rub was heard for the first time and was noted intermittently during the next 4 weeks Shortly thereafter a harsh precordial murmur was heard There were prominent left precordial pulsations and a thrill was thought to be present by some observers

A chest x ray at the time of his original hospitalization revealed an enlarged heart shadow consistent with pericardial effusion Subsequent films had revealed apparent progressive enlargement of the pulmonary artery This was first noted on Feb 25, 1958

The patient was admitted to the National Heart Institute on March 12, 1958 He did not appear to be ill The physical findings were not remarkable except for the examination of the chest There was a visible and palpable pulsation in the left second intercostal space and a minimal right ventricular lift was noted No friction rub was audible There was a Grade 3 systolic murmur maximal in the second and third left intercostal spaces This radiated into the neck and was also heard over the entire precordium A third heart sound was heard in diastole There was no diastolic murmur The pulmonic second sound was of normal intensity and split

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From the Clinic of Surgery National Heart Institute Bethesda Md
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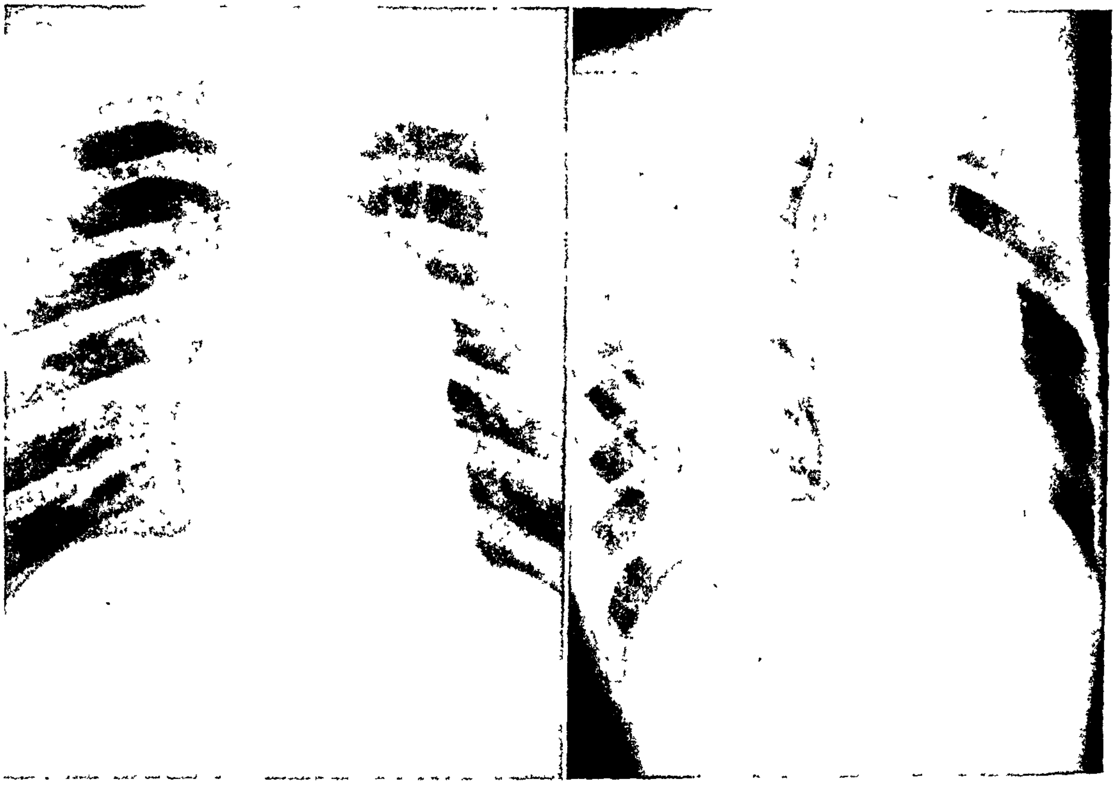
Fluoroscopic and roentgenographic examinations of the chest revealed a pulsatile mass in the left upper mediastinum in the region of the pulmonary artery (Fig. 1). There was no generalized cardiac enlargement but the right ventricle was slightly enlarged when viewed in the right anterior oblique projection. The vascularity of the left lung was considered to be slightly diminished as compared to the right. The electrocardiogram (Fig. 2) demonstrated a wide ST-T angle compatible with subsiding pericarditis. Comparison of the tracing with previous records showed a moderate rightward shift in the mean QRS axis, suggestive of early right ventricular hypertrophy. A right heart catheterization was carried out and the data obtained are summarized in Table I. There was a peak systolic pressure difference of 47 mm. Hg when the catheter was withdrawn from the pulmonary artery into the right ventricle. There was no evidence of a circulatory shunt.



A. B.

Fig. 1.—Posteroanterior (*A*) and right anterior oblique (*B*) chest x-rays. There is no generalized cardiac enlargement but the right ventricle is slightly enlarged. There is a mass in the left upper mediastinum in the region of the main pulmonary artery.

A selective angiocardiogram with right ventricular injection was performed following catheterization (Figs. 3 and 4). The right ventricle occupied a normal position. Lateral views revealed the right ventricular outflow tract and the main pulmonary artery to be compressed and displaced posteriorly by an extrinsic mass. The anteroposterior projection also showed deformity of both the main and left pulmonary arteries which were compressed and displaced. The mass visible in the plain films did not fill. A retrograde thoracic aortogram (Fig. 5) demonstrated that the ascending aorta was straightened and displaced posteriorly. The aortic lumen was not compromised and no aneurysm was present.

Following the studies outlined, the diagnosis of mediastinal tumor with compression of the right ventricle and pulmonary artery seemed established and operation was carried out on March 27, 1958. The chest was entered through a left anterolateral thoracotomy.

The pleural space was free and the lung appeared normal. The pericardium was markedly thickened and vessels on its surface were engorged and tortuous. When the pericardium was incised, a mass of gelatinous friable tumor extruded (Fig. 6). Three hundred grams of tumor were removed piecemeal but it was apparent that the tumor was infiltrating the *muscle of the right ventricle and left atrium as well as the pericardium.* After removal of the tumor (Fig. 7), the thrill previously palpable in the left pulmonary artery had disappeared and it was evident that the compression of the heart and great vessels had been relieved. The anterior mediastinum was palpably free of tumor and it was thought that the lesion had arisen and was confined to the pericardium

The patient's postoperative course was uncomplicated. The systolic murmur was markedly decreased immediately and gradually disappeared.

Pathologic examination of the tumor was carried out by Dr. Hugo Pribor. The tissue had a gelatinous consistency and was gray-red Areas of hemorrhage were apparent. On *microscopic examination several histologic patterns were evident (Fig. 8). In places, the* tumor cells were elongated and arranged in interlacing bundles. A moderate number of mitotic figures were present and there was considerable nuclear pleomorphism. Other areas

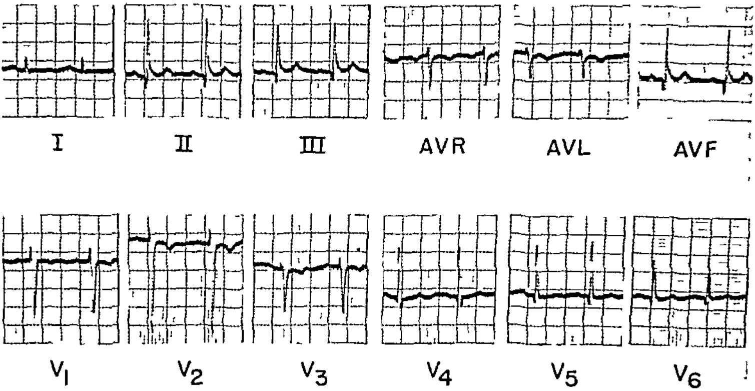


Fig 2.—The electrocardiogram demonstrates a wide ST-T angle compatible with subsiding pericarditis. There is a moderate rightward shift in the mean QRS axis suggestive of early right ventricular hypertrophy.

TABLE I. RIGHT HEART CATHETERIZATION

LOCATION	PRESSURE MM. HG. SYST./DIAST.	MEAN
Superior cava	9/6	7
Right atrium	9/2	6
Right ventricle	64/4	
Pulmonary artery	17/8	10
Wedge PA position	9/2	6
Brachial artery	125/75	85

NITROUS OXIDE TEST

LOCATION	BLANK	SAMPLE
Pulmonary artery	1.78	1.78
Brachial artery	—	7.24
Nitrous oxide index: 0%		

BODY SURFACE AREA: 1.96 M.² HEART RATE: 120/MIN.	
Cardiac output determination at rest*	
Ventilation, L./min.	7.78
O_2 Consumption, c.c./min.	327
R.Q.	0.71
A-V Difference, Vol. %	4.0
Systemic flow, L./min.	8.2
Arterial saturation	91.9 %
Pulmonary vascular resistance	58 d. s. cm.$^{-5}$

*Average of two determinations

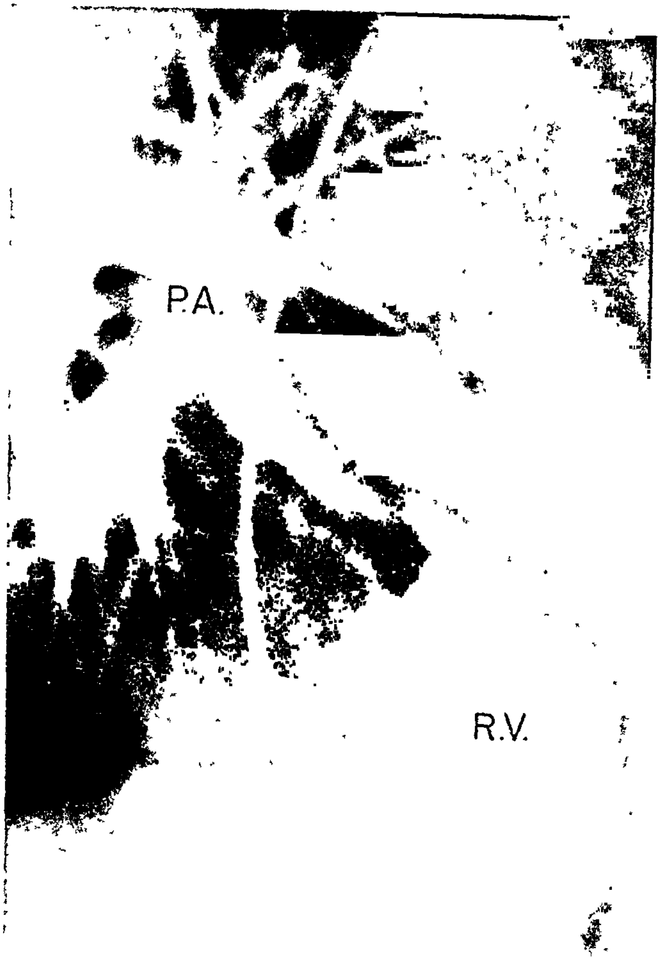


Fig. 3.—Selective angiocardiogram, lateral view: The right ventricular outflow tract and the main pulmonary artery are compressed and displaced posteriorly by an extrinsic mass. *RV*—Right ventricle. *PA*—Pulmonary artery.

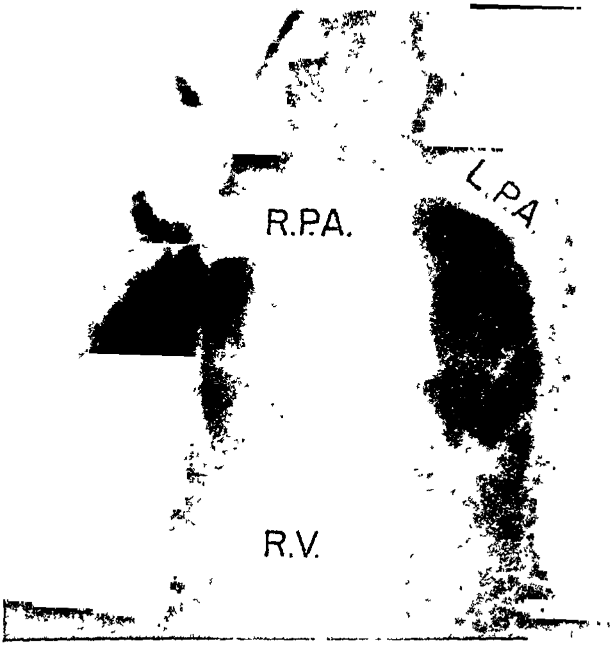


Fig. 4.—Selective angiocardiogram: anteroposterior view. There is a deformity of the pulmonary artery which is compressed and displaced upward. The mass visible in the plain films did not fill. *LPA*—Left pulmonary artery. *RPA*—Right pulmonary artery. *RV*—Right ventricle.

showed cuboidal tumor cells arranged in small nests with intervening vascular stroma. The tumor cells were often arranged around small blood vessels. The final pathologic diagnosis was primary mesothelioma of the pericardium. The patient was subsequently treated with x-ray therapy to the mediastinum and was discharged, free of symptoms, 3 weeks after operation.

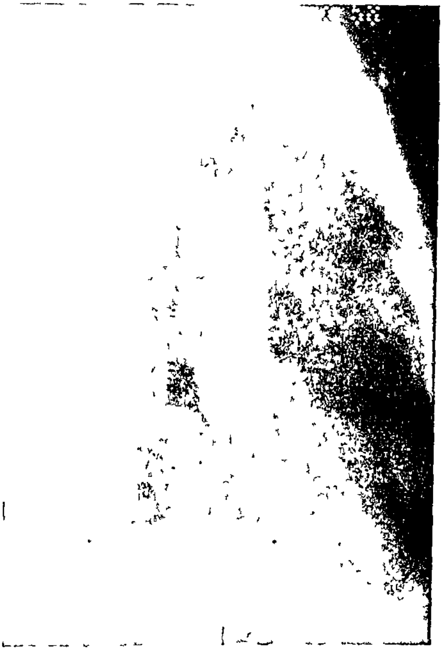


Fig. 5.—Retrograde thoracic aortogram. The aorta is straightened and displaced posteriorly. The aortic lumen is not compromised.

DISCUSSION

The patient described in the present report was the subject of much clinical speculation before the diagnosis was established. The presence of acquired pulmonic stenosis seemed clear on the basis of the physical findings and electrocardiograms. The initial history of an upper respiratory infection with fever and associated with radiographic and electrocardiographic evidence of pericarditis lead many to postulate a localized abscess or collection of sterile fluid as the nature of the mass. Others considered an aneurysm of the pulmonary artery or aorta to be more likely. The diagnostic studies demonstrated preoperatively that the mass was extrinsic to the vascular structures at the base of the heart but that the great vessels were displaced by it.

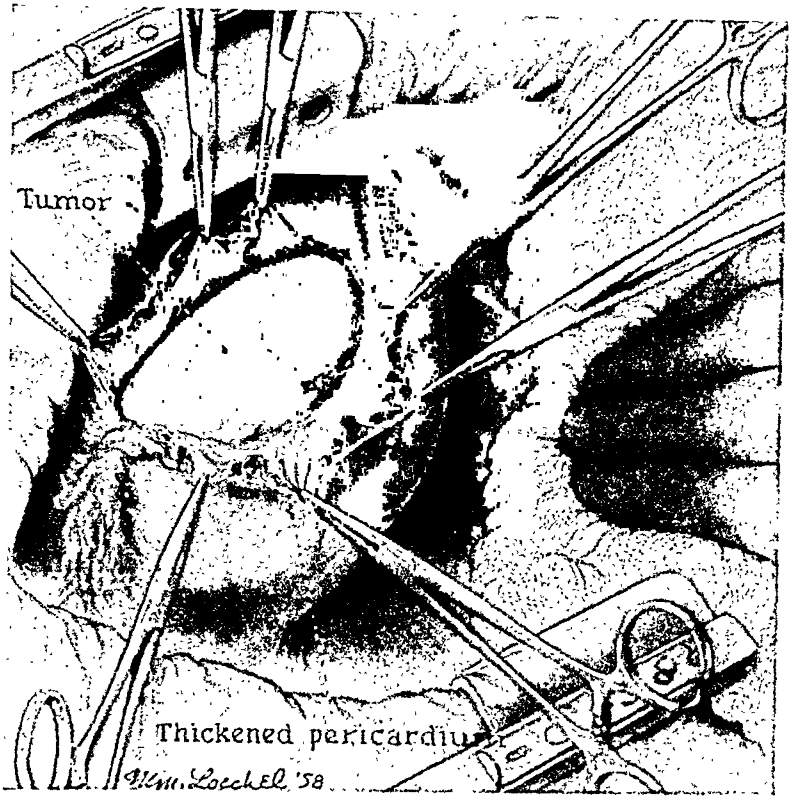


Fig. 6.—Operative appearance of the tumor, upon incision of the pericardium.

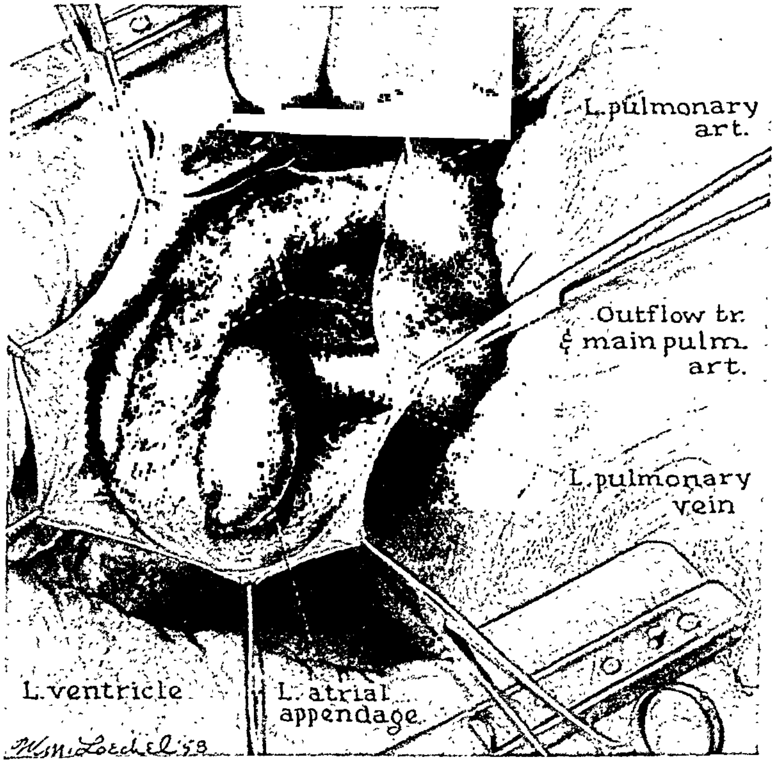


Fig. 7.—Following removal of the tumor, the compression of the pulmonary artery was relieved. The bed of the tumor with invasion of the outflow tract of the right ventricle and pulmonary artery is shown.

There have been two previous reports of patients in whom pulmonary stenosis apparently resulted from compression of the pulmonary artery by a tumor. The patient described by Fry[1] had a malignant teratoma. He had a palpable precordial thrill as well as a pulmonic systolic murmur. Cardiac catheterization was not performed and an angiocardiogram was inconclusive. However, both thrill and murmur were abolished by removal of the tumor but both signs later reappeared with recurrence of the tumor. Winter[2] recently reported complete studies in a patient with an anterior mediastinal tumor compressing the heart and producing a pulmonic systolic murmur. The patient was a 21-year-old white man who had a Hodgkin's tumor of the anterior mediastinum. The patient had a pulmonic gradient of 20 mm. Hg. At angiocardiography, a large mass was demonstrated compressing the pulmonary artery. The murmur disappeared after resection of the tumor.

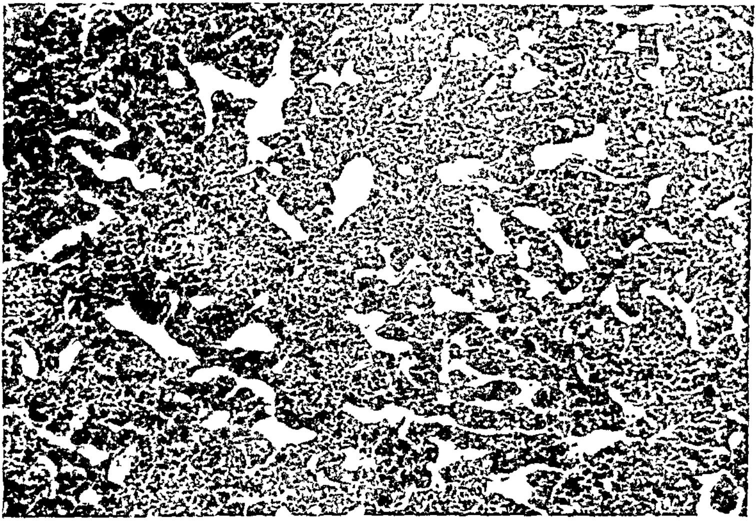


Fig. 8.—Photomicrograph of the tumor removed (hematoxylin and eosin stain × 143, reduced ⅕)

The rarity with which the pulmonary artery is compressed by a tumor is probably related to the fact that mediastinal tumors in general may enlarge laterally and need not encroach upon the heart and great vessels. The relatively few tumors arising within the pericardium usually result in an effusion and diffuse cardiac compression before a local constrictive lesion may manifest itself. Pericardial effusion was present early in the course of the present patient's illness but apparently resolved and the local manifestations of the enlarging tumor became evident.

SUMMARY

A patient is described in whom a primary mesothelioma of the pericardium compressed the pulmonary artery and caused the physical findings of obstruction to right ventricular outflow. A pressure gradient between the ventricle and pulmonary artery of 47 mm. Hg was demonstrated at cardiac catheterization. A selective right ventricular angiocardiogram demonstrated the extrinsic nature of the obstruction and its anatomic relations. Following excision of the tumor, the systolic murmur and thrill were no longer evident.

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TRACHEAL ADENOMA IN JUXTAPOSITION WITH A MEDIASTINAL BRONCHOGENIC CYST

Wilson Weisel, M.D., D. B. Claudon, M.D. and J. C. Dann, M.D.,
Milwaukee, Wis.

THE challenging clinical, diagnostic, surgical, and pathologic problems presented by a patient with a tracheal adenoma (carcinoid type) occurring in conjunction with a bronchogenic mediastinal cyst has provided the impetus for this case report In a review of the world literature we have not found an accounting of a similar report

CASE REPORT

G M (C H No 256671), a 49 year old white, widowed bank clerk, was admitted to the hospital Jan 17, 1958, because of intermittent hemoptysis of 5 years' duration She had noted a progressive increase in the amount of bleeding and expectoration of blood clots in the 2 weeks prior to admission

Past history revealed an appendectomy and oophorectomy performed in 1946 for non neoplastic lesions The family history was negative Physical examination demonstrated a healthy woman with a blood pressure of 150/90 mm Hg, a pulse rate of 80 and a respiratory rate of 20. A roentgenogram of the chest was reported as normal (Fig 1).

At bronchoscopy, a large polypoid tumor was found almost filling the tracheal lumen and arising from the left lateral wall, 3 to 4 cm above the carina From visual and tactile perception it was thought that a large globular portion of the tumor had residence outside the tracheal wall The intratracheal tumor was partially resected for biopsy. At second endoscopy performed a week later most of the remaining intratracheal lesion was resected

Because it was believed that a portion of the tumor was extraluminal, laminographic studies of the chest were made to delineate the left paratracheal area These roentgenograms were interpreted as demonstrating the presence of the suspected tumor (Fig 2) and, accordingly surgical excision of the tumor was planned

At a left thoracotomy, performed on Jan 29, 1958, utilizing a modified Carlens tube for an anesthetic airway,* the paratracheal mass, which could be felt medial and superior to the aorta, was identified as a cyst which was dissected from the trachea and removed

A three sided window, 2 cm in width, was cut in the trachea, leaving the membranous portion attached The area of the tracheal incisions corresponded to the former attachment of the cyst and the location of the intratracheal tumor

It was surprising to find that most of the tumor had actually been removed and there was no invasion of the tracheal wall The gross remnant of tumor in the mucosa was removed by stripping the mucosa from the cut portions of the tracheal cartilages The tracheal

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From the Departments of Surgery and Laboratory Medicine Columbia Hospital and the Marquette University School of Medicine Milwaukee Wis.

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*Dr J W Temple anesthesiologist

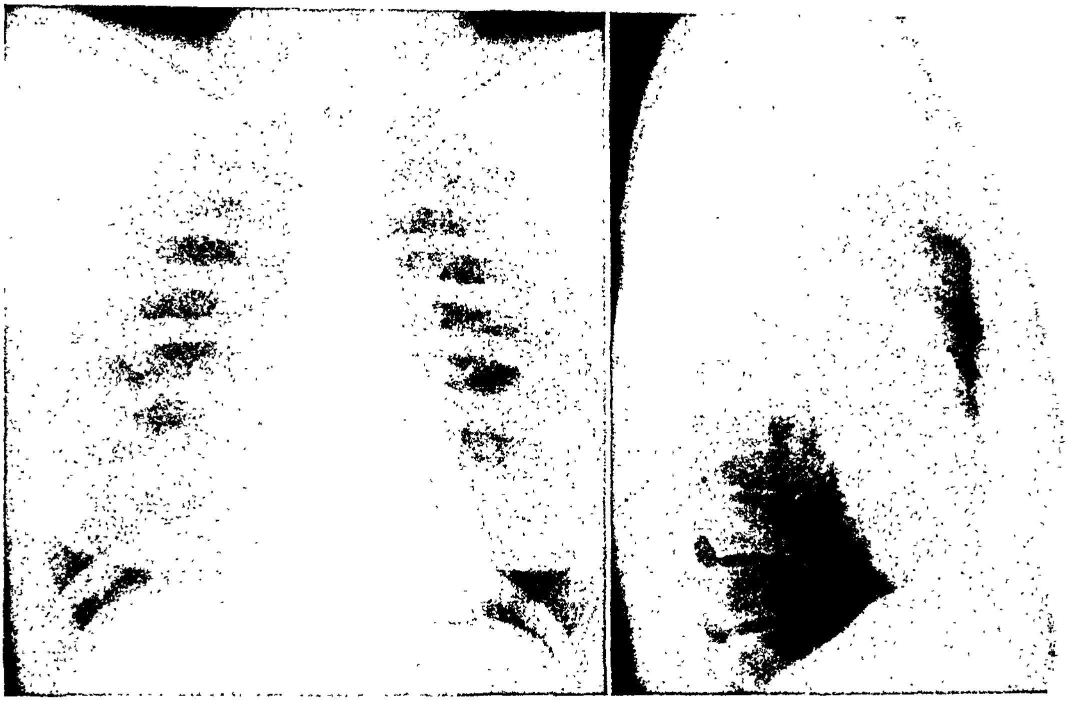

Fig. 1.—Posteroanterior and lateral thoracic roentgenograms taken on admission were interpreted as normal.

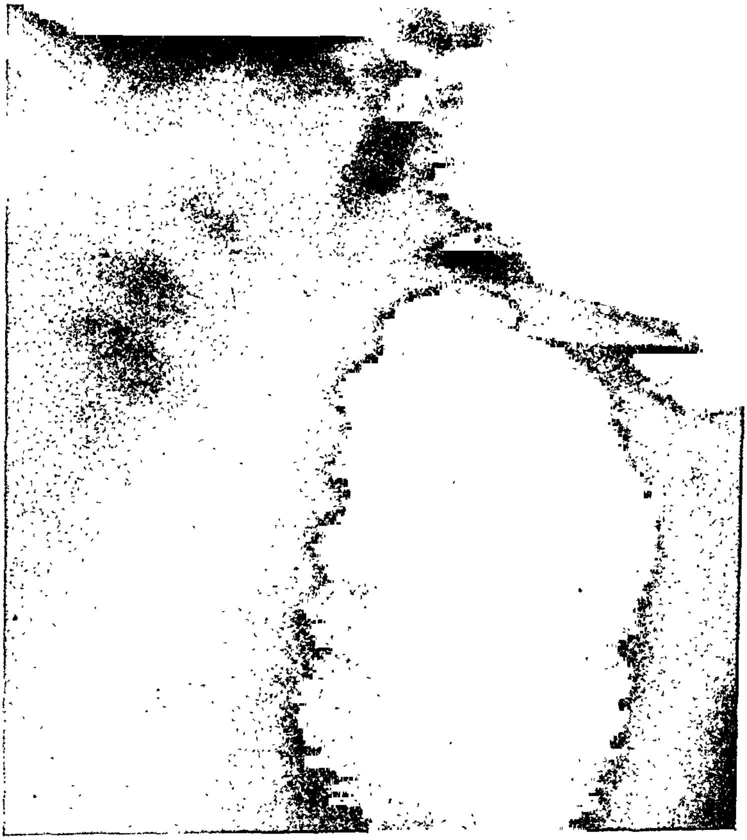

Fig. 2.—Laminogram of mid-thorax showing left lower tracheal and paratracheal mass.

wall was resected at the site of origin of the tumor and the tracheal defect was closed by a pedicled flap of pericardium which had been turned up from just above the diaphragm and was left attached over the great vessels. The flap was carefully sewn to the edges of the tracheal defect with interrupted 5-0 silk sutures.

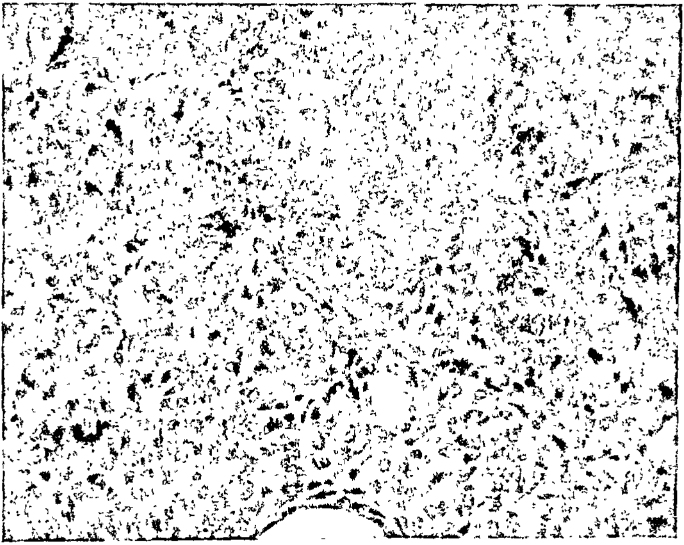

Fig. 3.—Photomicrograph (×200) of tracheal tumor showing epithelial cells arranged in anastomosing cords.

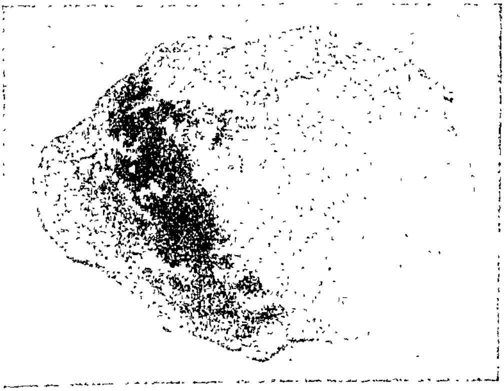

Fig. 4.—Photograph of mediastinal cyst.

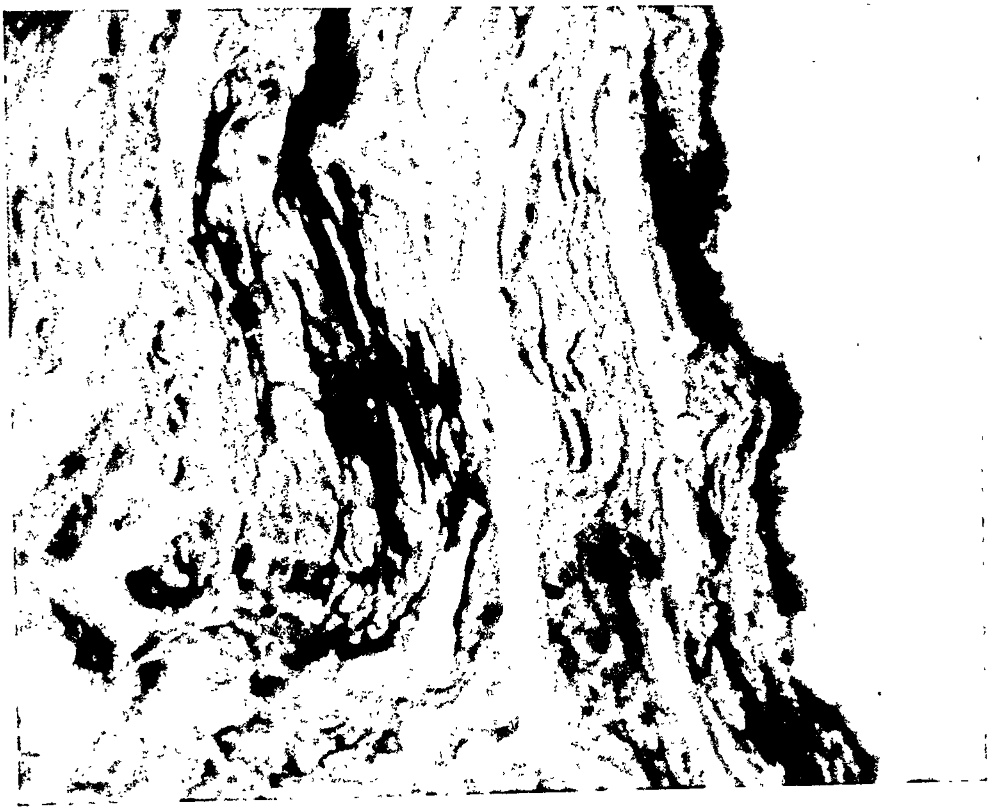

Fig. 5.—Microscopic section (×200) of cyst wall with elastic stain showing haphazardly arranged elastic fibrils.

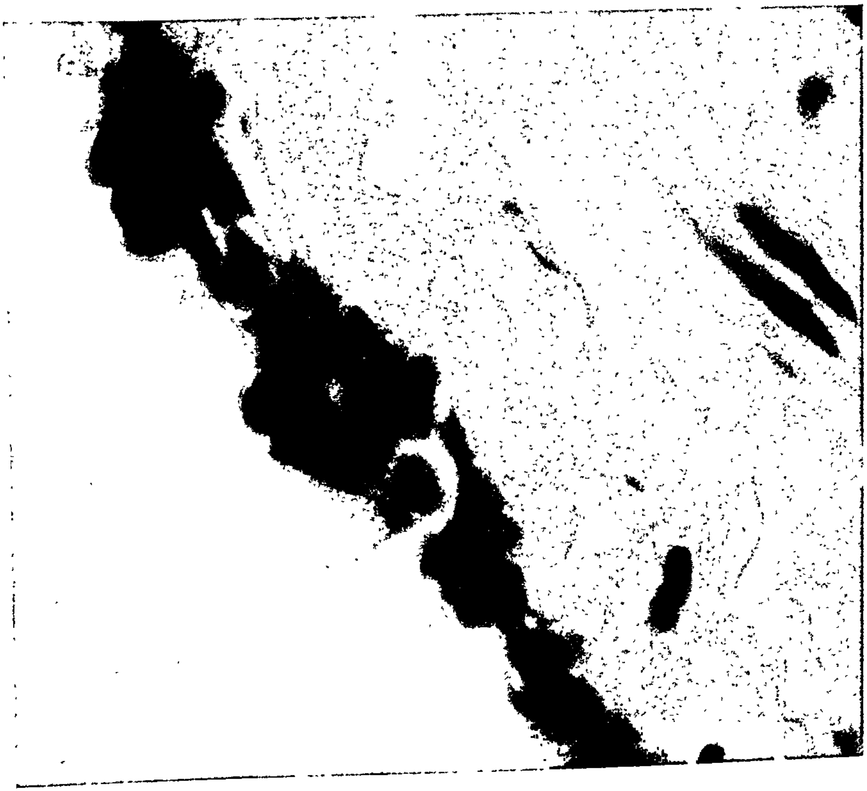

Fig. 6.—Photomicrograph (×850) of cyst lining demonstrating ciliated columnar cells.

The pleural space was drained by three catheters and the wound was closed with interrupted cotton sutures. The patient's convalescence was uneventful and she was discharged Feb. 12, 1958. She returned to work 10 days later. Follow-up studies have shown no symptoms nor signs referable to the respiratory system. Bronchoscopic examinations performed 3 and 6 months postoperatively have revealed a well healed, epithelized graft area. The only abnormality noted at endoscopy was some increased mobility of the wall in the graft area during expiration and coughing.

Pathologic Report.—The tracheal tumor received on three occasions in various sized pieces was characterized grossly as soft, brown tissue, the largest piece measuring 0.5 by 0.8 by 1.0 cm. On microscopic examination, the tissue was identified as from the inner wall of the trachea. The mucosa was normal, but the submucosa contained a well defined, non-encapsulated tumor composed of differentiated epithelial cells arranged in anastomosing cords (Fig. 3). The cells were of medium size with nuclei having vesicular chromatin. No evidence was seen of pleomorphism, mitoses, or anaplasia. A diagnosis of low grade adenocarcinoma ("tracheal adenoma"), carcinoid type, was made.

Part of the specimen received Jan. 29, 1958, was a thin-walled, spheroidal cyst with areolar tissue and muscle fragments attached to its surface (Fig. 4). The cyst measured 1.5 by 2.5 by 2.5 cm. and, when opened, was unilocular with a lining of smooth, gray, glistening tissue. It contained 7 ml. of clear amber fluid which on analysis had the following composition: 98 mEq./L. of sodium, 83 mEq./L. of chloride, 800 mg./100 ml. of protein, 27 mg./100 ml. of nonprotein nitrogen, less than 10 mg./100 ml. of sugar, and a pH of 8.

Histologic examination of the wall of the cyst showed an outer layer of areolar tissue containing occasional groups of fat cells, clusters of lymphocytes, and packets of fusiform smooth muscle cells. Elastic tissue stains demonstrated the presence of many elastic fibrils, singly and in haphazardly arranged interwoven collections (Fig. 5). No basement membrane was present. The cyst was lined by epithelial cells which underwent gradual transition in successive microscopic fields from cuboidal to columnar; the latter were frequently ciliated (Fig. 6). Many sections from numerous tissue blocks of the cyst wall disclosed the absence of cartilaginous plates, lymphoid follicles, and tissues of thymic, parathyroid, esophageal, gastric, or intestinal derivation. There was no evidence of extension of the tracheal tumor into the cyst wall.

DISCUSSION

The potential for extraluminal mediastinal extension of respiratory tract adenomas has been well documented[2, 5, 8] and confirmed by our own experience. The gross and microscopic characteristics of the tracheal tumor reported satisfied, in all respects, the well-defined criteria[5] for "carcinoid adenoma." The fact that a second lesion may simulate the endoscopic and radiologic features of mediastinal extension has been demonstrated by the patient described. The rarity of this coincidence is attested by our failure to find a similar case recorded, although a mediastinal cyst occurring in conjunction with an aortic aneurysm has been reported.[7] While the evidence suggests that, in this case, the neoplasm was completely removed, time alone will tell since local recurrence and appearance of metastases many years after operation have been recorded in patients with this disease.[8]

The anatomic features of this cyst, especially the presence of lining epithelium having occasional ciliated cells, were considered best explained by the interpretation that the structure was of bronchogenic origin. Derivation from the esophagus or other levels of the alimentary tract or foregut[1, 4, 6] was deemed unlikely. The absence of plates of cartilage or of seromucinous glands from the wall of the cyst has not been regarded as contradictory to the diagnosis but explainable on the basis that the cyst was derived from ectopic bronchiolar-directed cells. The nature of the fluid removed from the cyst was held consistent with this view, inasmuch as the anatomic position of the cyst and the character of its fluid were quite different from those described for cases of "ciliated esophageal cysts."[3]

In the repair of the tracheal defect, we have been favorably impressed by the pericardial graft. The pericardium has the advantage of being easily available, durable, and a conforming, living tissue with readily preserved blood supply. It has been previously used to reinforce bronchial stump closure and our experience has shown it to be an excellent substance for repair of experimental heart defects in animals.

SUMMARY AND CONCLUSIONS

1. A patient is reported in whom a tracheal "adenoma" occurred in juxtaposition to a mediastinal bronchogenic cyst.

2. The diagnosis of extratracheal extension of the "adenoma" was suspected by endoscopic and roentgen examination. The correct diagnosis was made at thoracotomy.

3. A pedicled pericardial graft was used to close the tracheal surgical defect. Follow-up bronchoscopic observations have demonstrated excellent healing and apparent epithelization of the graft area.

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Erratum

In the article, "Mitral Insufficiency With Compression of the Left Main Bronchus Treated by Open-Heart Surgery," by Drs. David R. Murphy, Anthony R. C. Dobell, Gordon M. Karn, and James E. Gibbons, in the March issue of the Journal on page 322, Figs. 2 and 3 should be reversed, the legends remaining as they are.

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Original Communications

ANASTOMOSIS OF SUPERIOR VENA CAVA AND PULMONARY ARTERY IN THE SURGICAL TREATMENT OF CERTAIN CONGENITAL DEFECTS OF THE HEART

A. N. Bakulev and S. A. Kolesnikov,** Moscow, U.S.S.R.*

In THE JOURNAL OF THORACIC SURGERY, April, 1958, F. Robicsek, R. Magistro, E. Foti, L. Robicsek, and P. Sanger published an article entitled "Vena Cava Pulmonary Artery Anastomosis for Vascularization of the Lung," an experimental study in dogs, which is of considerable theoretical interest, and undoubtedly has great practical significance. In June, 1957, one of the authors of this paper (A. N. B.) reported similar experimental studies, and presented clinical applications of this operation at the International Medical Congress in Turin, Italy.

At the present time, the operation of placing an anastomosis between the superior vena cava and the pulmonary artery is fairly widely used in a number of surgical institutions of the Soviet Union (Institute of Thoracic Surgery of the Academy of Medical Sciences of U.S.S.R., Vishnevsky's Institute of Surgery, and at the Central Institute of Post-graduate Studies, among others). This operation proved to be effective in cases of congenital heart disease with decreased pulmonary circulation and, in many cases, is undoubtedly superior to anastomoses between the aorta and the pulmonary arteries (Potts, Blalock, Taussig). In the present paper we should like to share with our American colleagues the experience gained in this field.

From the Institute of Thoracic Surgery, Academy of Medical Sciences of U.S.S.R., Moscow, U.S.S.R.

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*President, Academy of Medical Sciences of U.S.S.R.

**Doctor of Medical Science.

As early as 1951, one of the authors (A. N. B.) performed experimental and clinical anastomoses between the superior vena cava and the pulmonary artery for the surgical treatment of Fallot's tetralogy. He thought that this operation would decrease the overloading of the right heart and would remove the extra load on the left heart and other complications caused by the creation of the artificial arterial pathway, and that it would present fewer technical difficulties.

Independently of this, the Vishnevsky Institute of Surgery published, in 1956, a report on an experimental study which proved this operation to be possible and useful (N. K. Galankin).

On April 3, 1956, at the Institute of Thoracic Surgery of the Academy of Medical Sciences of U.S.S.R., the first anastomosis between the superior vena cava and the pulmonary artery had been made successfully in a boy of 15 (Prof. E. N. Meshalkin). The patient's condition began to improve rapidly following the operation. Cyanosis disappeared completely after 3 days. In a fortnight's time, hemoglobin content of the blood dropped from 130 per cent to 80 per cent. In a month's time, oxygen saturation figures of the arterial blood rose from 75 per cent to 90 per cent. The patient was discharged in good condition, which is maintained to this day. Since then 41 such operations have been performed at the Institute of Thoracic Surgery.

As the technique of the operation has been described in detail before (E. N. Meshalkin, 1956; N. K. Galankin and co-workers, 1957), we shall deal with it but briefly.

To facilitate dissection of the blood vessels a ¼ per cent solution of Novocain is injected into the lung hilum and the mediastinum along the superior vena cava. The mediastinal pleura is incised longitudinally above the superior vena cava and vein is exposed by blunt dissection some 5 to 6 cm. above its union with the pericardium. The pericardium is then incised longitudinally and the intrapericardial section of the vein is exposed as far down as its union with the right ventricle. The azygos vein is tied and severed. Following this, the right branch of the pulmonary artery is dissected out as far as its point of emergence from the main trunk; thick silk stays are placed on the upper and lower lobar branches of the artery to prevent the blood reflux from the lung. The artery is then tied at its point of emergence from the main trunk by double silk ligature and cut (Fig. 1). As most of the disorders of hemodynamics, leading to cerebral hypoxia, are related to the temporary occlusion of the superior vena cava, all manipulations on the latter are performed last and must be carried out with utmost speed. A hook-shaped clamp is placed on the superior vena cava distal to the site of the proposed anastomosis. The vein is then tied where it joins the right atrium and cut above the ligature. In order to speed up and facilitate ligation we use a special stitcher which places automatically two rows of tantalum staples on the superior vena cava (Fig. 2).

An end-to-end anastomosis is then placed between the peripheral ends of the superior vena cava and the pulmonary artery with the aid of continuous, U-shaped, everting sutures first on the posterior, then on the anterior wall of the anastomosis (Figs. 3 and 4). Once the vein clamp and the artery stays are removed no bleeding is seen as a rule, some oozing of blood through the needle punctures may be observed. It stops of its own accord. Once the clamp is off, one can observe good filling of the anastomosis and the branches of the pulmonary artery. Increased filling and tension of the superior vena cava diminish as soon as the anastomosis begins to function, although they still remain more marked than before the placing of the anastomosis.

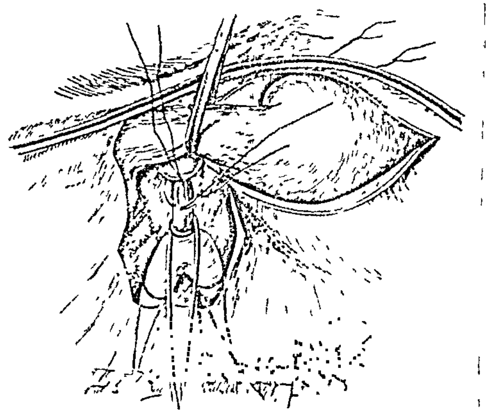

Fig. 1

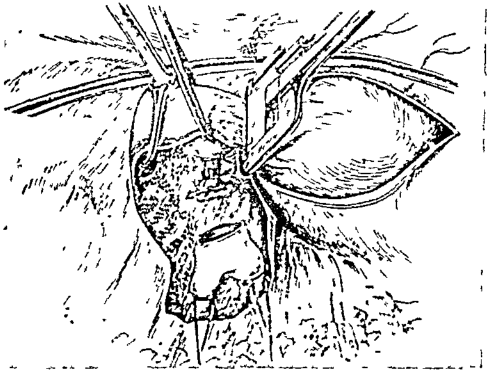

Fig. 2

Fig. 1.—The right branch of the pulmonary artery and the superior vena cava have been dissected out. The latter is pulled upward with the aid of a rubber tube passed around it. The pulmonary artery is dissected far into the posterior mediastinum, up to the bifurcation.

Fig. 2.—The pulmonary artery has been sectioned. Its tied stump is seen well inside (in the posterior mediastinum). The superior vena cava is clamped with a hooked clamp (left) and sutured by means of a mechanical stitcher (right).

As can be seen from the above description, the technique has no insuperable difficulties and the operation can be performed by a surgeon who has mastered vascular sutures. However, it is impossible to assess the difficulties and dangers of the operation on the basis of experimental evidence alone.

It must not be forgotten that these operations are performed on very ill patients with complicated lesions of the heart and marked myocardial changes.

Fig. 3.

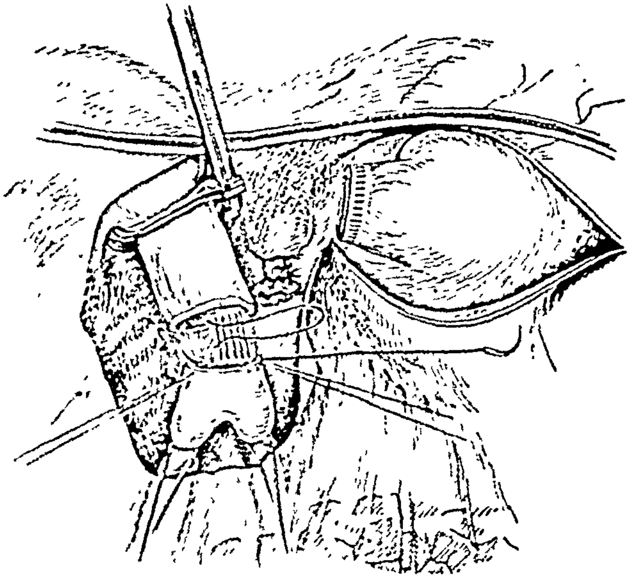

Fig. 4.

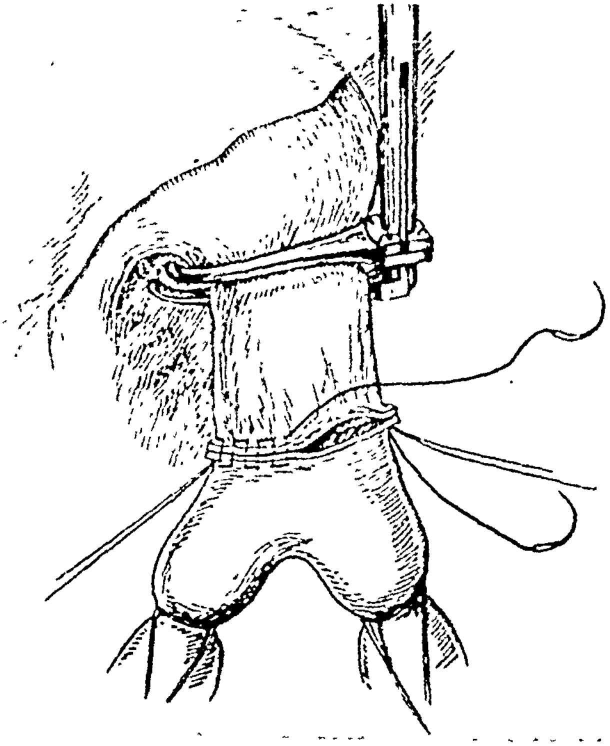

Fig. 3.—The moment of suturing the distal ends of the superior vena cava and the right branch of the pulmonary artery. After placing two U-shaped stays at the corners, the posterior walls of the vessels are sutured by means of a continuous, U-shaped, everting suture.

Fig. 4.—The posterior wall suture has been tightened and fastened by tying the thread to the corner stays. The moment of suturing the anterior walls of the vessels by a continuous, U-shaped, everting suture.

Marked hypoxia, affecting the functions of all the organs, including the brain, constitutes the most severe disorder in these diseases. Every manipulation that decreases the oxygenation of blood or upsets the circulation in these patients will be dangerous. Unfortunately, a number of such disorders will arise during the operation just described. Besides the significance of surgical trauma, especially during the dissection of the superior vena cava and the pulmonary artery, two particularly dangerous moments have to be mentioned.

These are, first of all, the occlusion [illegible] of the right pulmonary artery, leading to a considerable drop in [illegible] saturation of the blood in the already very hypoxic patient. Second, the [illegible] prolonged [illegible] of the superior vena cava, which leads to [illegible] congestion in the upper half of the body, causes tissue edema and at times [illegible] metabolism of the brain.

Observation of patients during the [illegible] changes, especially after the clamping [illegible] superior [illegible] pressure in all these patients [illegible] the pulmonary artery are being [illegible] out [illegible] cava causes no further drop [illegible] the venous blood [illegible] shoots up to 500 to 600 mm. H [illegible] Oxygen [illegible] the dissection of the major vessels which is [illegible] clusion during this stage of the operation [illegible] marked drop when the pulmonary artery is tied [illegible] perior vena cava is clamped. At this [illegible] from 90 per cent to 30 per cent and [illegible] perior vena cava is off and then [illegible] the blood oxygen figures begin [illegible]

Electroencephalographic [illegible] the presence of typical changes [illegible] hypoxia and hypercapnia of the [illegible] ters progresses. Voltage is [illegible] After removal of the clamp [illegible] disappear gradually.

Thus, it must be admitted [illegible] the moment when the superior [illegible] at its highest. Marked cyanosis [illegible] exophthalmos and, [illegible] the upper half of the body is [illegible] if all goes well, disappears [illegible] and G. M. [illegible] cava up to 40 [illegible] data. Patients [illegible] Hence [illegible]

It is [illegible] between [illegible] operation [illegible] without due consideration of the severity of each patient's condition, and the degree of severity is not always easy to assess, let alone to be able to make a comparison in different patients with the use of the methods now available.

If we exclude deaths due to accidental causes and imperfect technique, the clamping time of the superior vena cava in patients who died after the operation varied between 13 and 26 minutes. On the other hand, in patients who had stood the operation well the clamping time varied between 14 and 30 minutes. Minimum clamping time in our series of operations was 13 minutes, maximum—30 minutes.

To cut down on the time required for the placing of anastomosis, special rings made of stainless steel (Donetsky) are used at the Vishnevsky Institute of Surgery. We use for the same purpose a blood vessel stitcher constructed by the Institute of Surgical Instruments and Apparatus of the Ministry of Health of U.S.S.R. With the aid of this apparatus, it is possible to place the anastomosis in 5 to 6 minutes. This method, besides saving time, has definite advantages over the manual suturing of vessels by leaving behind a material that causes but minimum reaction in tissues (tantalum), by ensuring perfect approximation of the intima of the vessels sutured without the sutures penetrating into the lumen of the blood vessels and, mainly, by creating an obstacle to the subsequent expansion of the anastomosis as the blood vessels grow in size.

An excerpt follows from the case history of a child, aged 5, operated upon for Fallot's tetralogy by the method just described.

CASE REPORT

The child, M., was admitted to the Institute of Thoracic Surgery on Jan. 18, 1958, complaining of dyspnea and marked cyanosis. Diagnosis of heart disease had been made a few days after birth. Dyspnea and cyanosis increased as the child grew. Dyspnea often forced him to squat.

Examination revealed the presence of cyanosis of lips and fingernails; clubbed fingers; respirations, 24; pulse, 104; blood pressure 100/75 mm. Hg; a rough, systolic murmur over the precordial region with maximum intensity in the third and fourth interspaces to the left of sternum; murmur radiates freely along the cervical blood vessels; hemoglobin, 134 per cent (23.3 Gm.); red blood cells, 6,500,000.

An electrocardiogram showed impairment of intracardiac conduction, myocardial lesions of the right ventricle, and sinus tachycardia.

A roentgenogram of the chest (Fig. 5) showed light lung markings, heart enlarged in transverse diameter, heart waist markedly accentuated, apex displaced to the left, dextroposition of the aorta. Angiocardiography and cardiac catheterization confirmed the diagnosis of Fallot's tetralogy and infundibular stenosis of the pulmonary artery of the tubular type.

Anastomosis between the superior vena cava and the pulmonary artery was made, which was all the more indicated as the patient had dextroposition of the aorta. The technique described above was adhered to. The anastomosis was made with the aid of a stitcher with tantalum staples. The anastomosis was over 1 cm. in diameter and its function was good. The operation lasted 1 hour and 30 minutes.

Hemodynamic and other physiologic changes during the operation were typical for operations of this type. While the anastomosis was being placed, the blood pressure fell from 90/70 to 80/50 mm. Hg. Oxymetry readings went down from 84 per cent to 50 per per cent. After ligation of the pulmonary artery, the electrocardiogram showed moderate hypoxia, inconstant group extrasystoles and slowing of the pulse from 150 to 128 per minute.

At the moment of clamping of the superior vena cava, the electroencephalogram registered marked hypoxia and hypercapnia lasting 20 to 25 seconds. During the placing of the anastomosis, signs of progressive depression of the nervous centers was evident with decrease of voltage and appearance of silent zones. With the clamp off, signs of cerebral hypoxia and hypercapnia decreased in from 1 to 1.5 minutes and gradually disappeared entirely after 4 to 5 minutes.

The patient was taken to the postoperative ward with a blood pressure of 120/90 mm. Hg. There was considerable edema of the face which persisted for 24 hours.

The postoperative course was smooth. Cyanosis began to decrease from the first postoperative day and disappeared entirely by the time of discharge. Hemoglobin dropped from 136 per cent to 95 per cent. The child was discharged 17 days after operation in satisfactory condition.

As will be seen from Figs. 6 and 7 the lung markings, as compared with the preoperative film (Fig. 5) have increased due to improved circulation of the right lung; the same may be observed when comparing it with the left side.

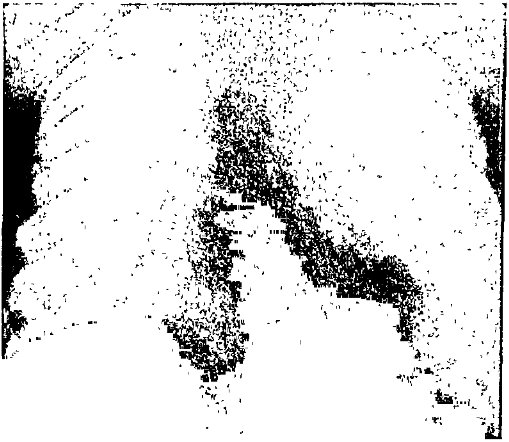

Fig. 5.—Chest roentgenogram of Patient M., aged 5, before operation.

Note the shadows of metal staples, forming a circular shadow consisting of separate staples, which project themselves against the seventh and eighth thoracic vertebrae. The shadow corresponds to the site of the vascular anastomosis. Another shadow below corresponds to the sutured stump of the proximal part of the superior vena cava.

Out of 41 patients operated upon, 14 died during the operation or in the postoperative period (4 on the operating table), 7 in the first 24 hours postoperatively, 1 on the second day, 1 on the third day, and 1 on the forty-fifth day. This relatively high mortality rate may be explained not so much by the surgical trauma itself as by the imperfect technique and anesthesia, which, during the period described, were being perfected for the above operation. Thus, in 6 cases death supervened on the operating table through acute hemorrhage, or else in the immediate hours following the operation. In 2 cases, death without due consideration of the severity of each patient's condition, and th degree of severity is not always easy to assess, let alone to be able to make a com parison in different patients with the use of the methods now available.

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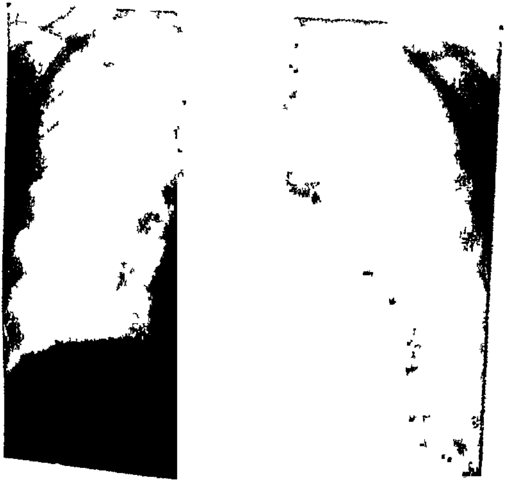

Fig. [illegible].—Chest roentgenogram of Patient M., aged 5, before operation.

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Distant results were checked by us in 16 children up to 2 years postoperatively. Out of 16 children, 14 had good results and in only 2 was the improvement slight. It should be noted that these 2 children belonged to the group with more severe disease. All the 14 children who showed good results were enabled to walk and run freely (what they could not do prior to operation); in 8 of them slight dyspnea supervenes upon running, but this does not seem to bother them much; 5 children use a bicycle. In 6 children, clubbing of fingers disappeared entirely and in 8 the sign has markedly decreased. The size of the heart has not altered in any of the 14 children. Auscultatory data have remained the same as before the operation. It is important to note that in no single instance of good postoperative results was there any subsequent deterioration which is in contrast to what we have seen in a number of cases subjected to the Blalock-Taussig or Potts anastomosis.

Although our experience with the surgical treatment of congenital heart disease with insufficiency of pulmonary circulation by anastomosing the superior vena cava and the right branch of the pulmonary artery is modest, we feel justified in drawing the following conclusions.

1. The placing of a vena cava-pulmonary anastomosis for the treatment of patients with insufficiency of pulmonary circulation has demonstrated its usefulness and effectiveness in the treatment of such cardiac lesions.

2. This operation is not excessively complicated and can be performed by any thoracic surgeon who has mastered the technique of vascular suture.

3. The advantages of this operation as compared to the interarterial anastomoses are as follows: (a) decrease in the overload of the right ventricle; (b) decrease of the overload in the system of the pulmonary artery, which leads to the subsequent sclerosis of the pulmonary vessels; (c) considerable increase of the quantity of oxygenated blood; (d) avoidance of recirculation of the blood through the interarterial anastomosis; and (e) avoidance of endarteritis, which supervenes occasionally at the site of interarterial anastomosis.

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CEREBRAL CHANGES DURIN CARDIORESPIRATORY BYPASS USING THE HELIX RESERVOI BUBBLE OXYGENATOR

Nazih Zuhdi, M.D., Walter Joel D.,** John Carey, M.D.,*** Mary Lou Faggella, and Allen Greer, M.D.,* * Oklahoma City, Okla.*

ON examination of the brains dogs following partial perfusion with a DeWall bubble oxygenator the arterial catheter placed in a carotid artery, Giannelli, Molthan, Best, l. and Kirby[1] found lesions characteristic of embolism and infarction in a Disquieted by these findings, the following experiments were performed order to study the gross and microscopic changes that occur following tot diopulmonary bypass using the helix reservoir bubble oxygenator.

METHODS

Eight mongrel dogs, weigh from 15 to 25 Kg., were anesthetized Pentothal sodium and the trach was intubated. Following right thoracotomy, plastic catheters were inserted o the superior and inferior venae cavae and occluding tapes placed around t m. The arterial catheter was placed in either the carotid or femoral artery. A DeWall-Lillehei bubble oxygenator[2] was primed with heparinized blood. The arterial filter† was not used during the last four perfusions. Heparin (2 mg./Kg.) was injected intravenously, perfusion was carried out for 30 minutes at a flow rate from 40 to 50 c.c./Kg. of body weight, and an interatrial defect created and closed. Protamine sulfate (4 mg./Kg.) was given at the end of the perfusion.

Seven animals were sacrificed one week following perfusion and one dog expired on the first postoperative day. The brains were carefully removed and immersed in neutral 10 per cent formalin for 3 weeks. The meninges were inspected, surface cortical alterations noticed (edema, changes in sulci and gyri, softening and hemorrhage), and the base of the brain was examined. Coronal sections were cut to include the cortex, basal ganglia, brain stem, thalamus, hypothalamus, medulla and cerebellum. Hematoxylin and eosin, gallocyanin (Einarson), Klüver, Holzer, and Bodian stains were used.

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*Present address: 426 NW 12, Oklahoma City, Okla.

**Professor of Pathology, Oklahoma University Medical School, Oklahoma City, Okla.

***Instructor in Surgery, Oklahoma University Medical School, Oklahoma City, Okla.

****Assistant Professor of Surgery, Oklahoma University Medical School, Oklahoma City, Okla.

†Double metal filter graciously supplied by Abbott, North Chicago, Ill.

RESULTS

On gross examination, no cerebral changes were seen in any dog. Microscopically, no lesion characteristic of embolism or infarction could be detected in any brain. However, cellular alterations were noticed in 2 dogs (No. 3 and No. 8). They were few, slight, and preponderantly present in the ganglion

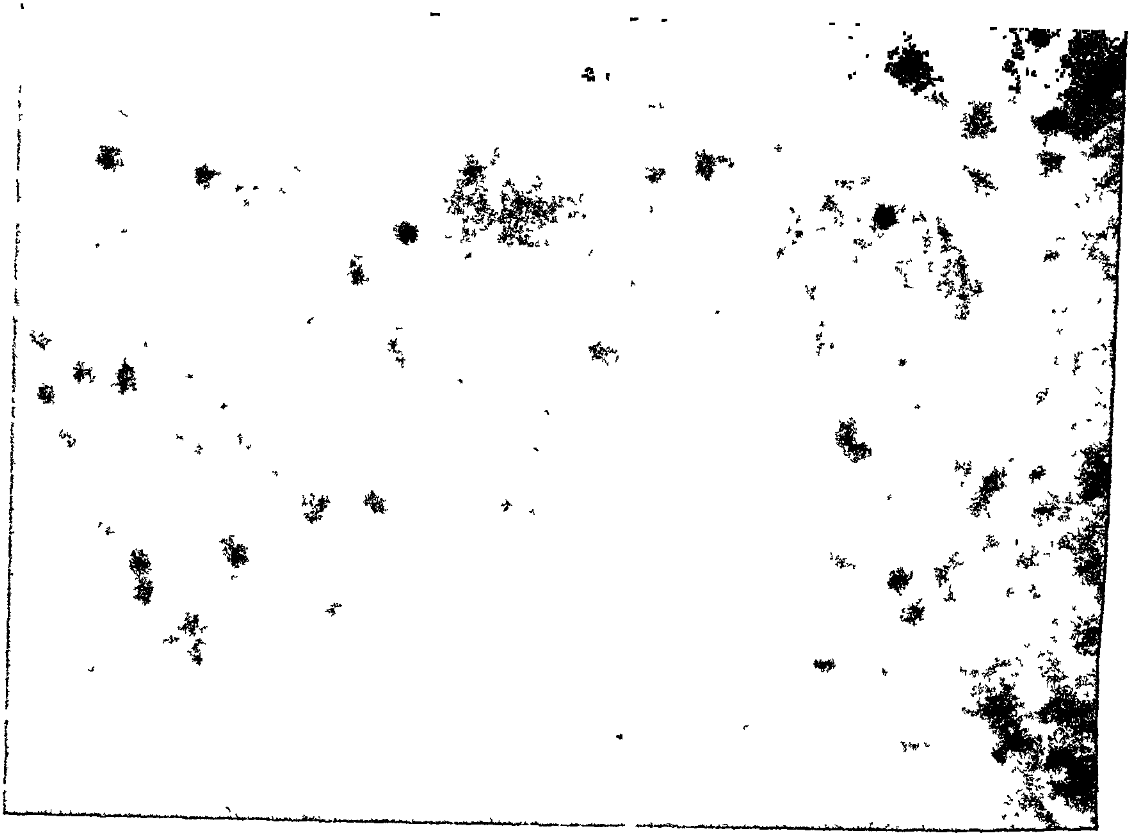

Fig 1.—Swollen ganglion cells in some areas in the brain of Dog No. 3. Note the presence of nuclei.

TABLE I. SUMMARY OF CEREBRAL CHANGES IN 8 DOGS PERFUSED USING THE METHOD OF LILLEHEI

	DOG NUMBER	GROSS CHANGES	MICROSCOPIC EMBOLISM OR INFARCTION	OTHER MICROSCOPIC CHANGES
Group 1. Arterial catheter in carotid artery; filter used	1	None	None	Slight hyperemia of meningi
	2	None	None	Mild satellitosis around ganglion cells in some areas of cortex
Group 2. Arterial catheter in femoral artery; filter used	3	None	None	Some swollen ganglion cells (Fig. 1)
	4	None	None	None
Group 3. Arterial catheter in femoral artery; no filter used	5	None	None	None
	6	None	None	None
	7*	None	None	None
	8	None	None	Some angulated ganglion cells (Fig. 2)

*Died the first postoperative day

cells of the motor nuclei in the brain stem They consisted of ballooning of ganglion cells in some areas (Fig 1) and shrinkage and angulation in others (Fig 2) However, no demyelinization was detected with Kluver stain and no gitter cells, "fat droplet containing phagocytes" were seen No changes were noticed in the cerebellum, especially in the Purkinje cells The findings are summarized in Table I

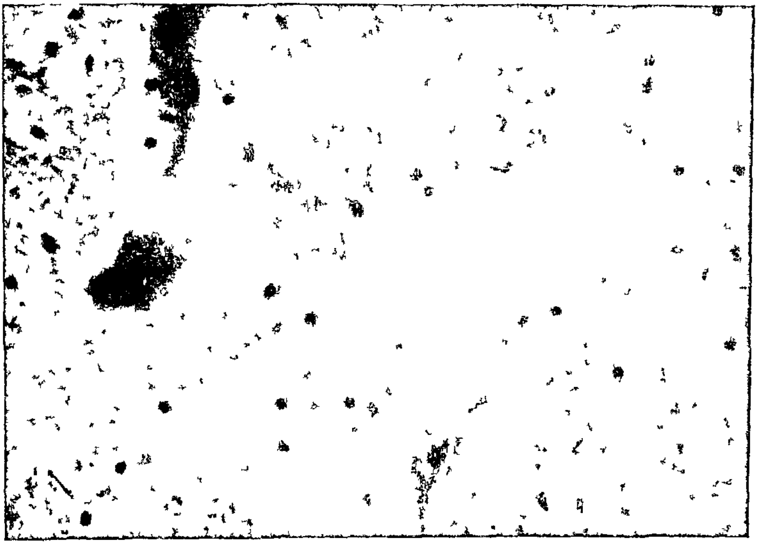

Fig 2 —Shrunken and angulated ganglion cells as seen in few areas in the brain of Dog No 8

DISCUSSION

Under the conditions prevailing during these experiments, lesions characteristic of infarction or embolism could not be detected There were no areas of softening, liquefaction, or hemorrhage The site of the arterial catheter or the absence of a filter did not affect the findings These results are at a considerable variance with those reported by Giannelli and associates[1] It is possible that the alterations seen by these workers were due to the longer duration of their experiments

Hypoxic changes in the brain are best noticed in the Betz cells, Purkinje cells, and in the ganglion cells of the hippocampus (Sommer's section) These particular cells were well preserved The observed changes were few, slight, and in 2 dogs only They are probably related to the low perfusion flows Disruption of the blood brain barrier as described by Hodges and his co workers[3] is considered a more sensitive index of cerebral alteration than are histologic changes The absence of demonstrable cerebral air embolism by the vacuum technique of Schubert has been discussed by Heimbecker.[1] Certainly the absence of significant histologic changes adds some reassurance to the already proved safety of the DeWall bubble oxygenator.

SUMMARY

A DeWall bubble oxygenator did not cause any detectable gross changes in the brain of 8 dogs perfused for 30 minutes at a flow rate from 40 to 50 c.c./Kg. Microscopically, no lesions characteristic of embolism or infarction were seen, whether the arterial catheter was placed in the carotid or femoral artery and whether or not a filter was used. Changes compatible with hypoxia were observed in 2 dogs.

Deepest appreciation is expressed for the help of Dr. Robert Faggella, Mrs. Peggy Johnson, and Miss Jerry Tucker.

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NEW METHOD FOR SYSTEMIC ARTERIAL PERFUSION IN EXTRACORPOREAL CIRCULATION

Luis E Nuñez, M D , and Charles P Bailey M D , Philadelphia, Pa

Ever since extracorporeal circulation for open heart surgery was first initiated, a critical question has been the technique for establishment of an adequate perfusion of the arterial system

For this purpose, cannulization of the subclavian artery and/or the femoral artery has been performed, but limitations have been encountered occasionally in their use due to the small diameter of these arteries, especially in infants Even in adults, the largest femoral artery has only allowed the passage of a No 28 Fr Bardic catheter The problem has been accentuated by the recent trend toward higher flows in an attempt to achieve a near normal volume of perfusion In addition, there is no doubt that a small catheter may create turbulence of the blood due to the high velocity necessary inside the catheter and, as a consequence, hemolysis of the red cells and destruction of the other sensitive elements of the blood may become manifest

The necessity for finding another method of arterial perfusion was patent Suture of a side arm to the aorta as suggested by Dodrill[1] appears too time consuming Consequently, a new instrument (Fig 1) for direct aortic cannulization has been designed by one of us (Luis E Nuñez) and found useful in actual clinical trial This clamp* permits quick insertion of a large catheter into the thoracic aorta The instrument has been constructed in various sizes to permit the use of catheters from No 12 Fr to No 40 Fr With these clamps, full circulatory flow rates are attainable in all cases from the infant to the adult

*This clamp has also been found useful when an emergency bypass is re*quired This occurred recently during a nonopen heart operation on a patient in whom cardiac arrest occurred In a very short time a bypass was established and the arrest overcome A slight modification of this clamp permits rapid insertion of a catheter through the atrial wall for caval cannulization

TECHNIQUES

Insertion of the catheter with the clamp is simple and requires only a fraction of the time needed for femoral or subclavian artery cannulation When the chest has been opened (to perform the main operation), an ordinary

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*Made by George Pilling of Philadelphia, Pennsylvania

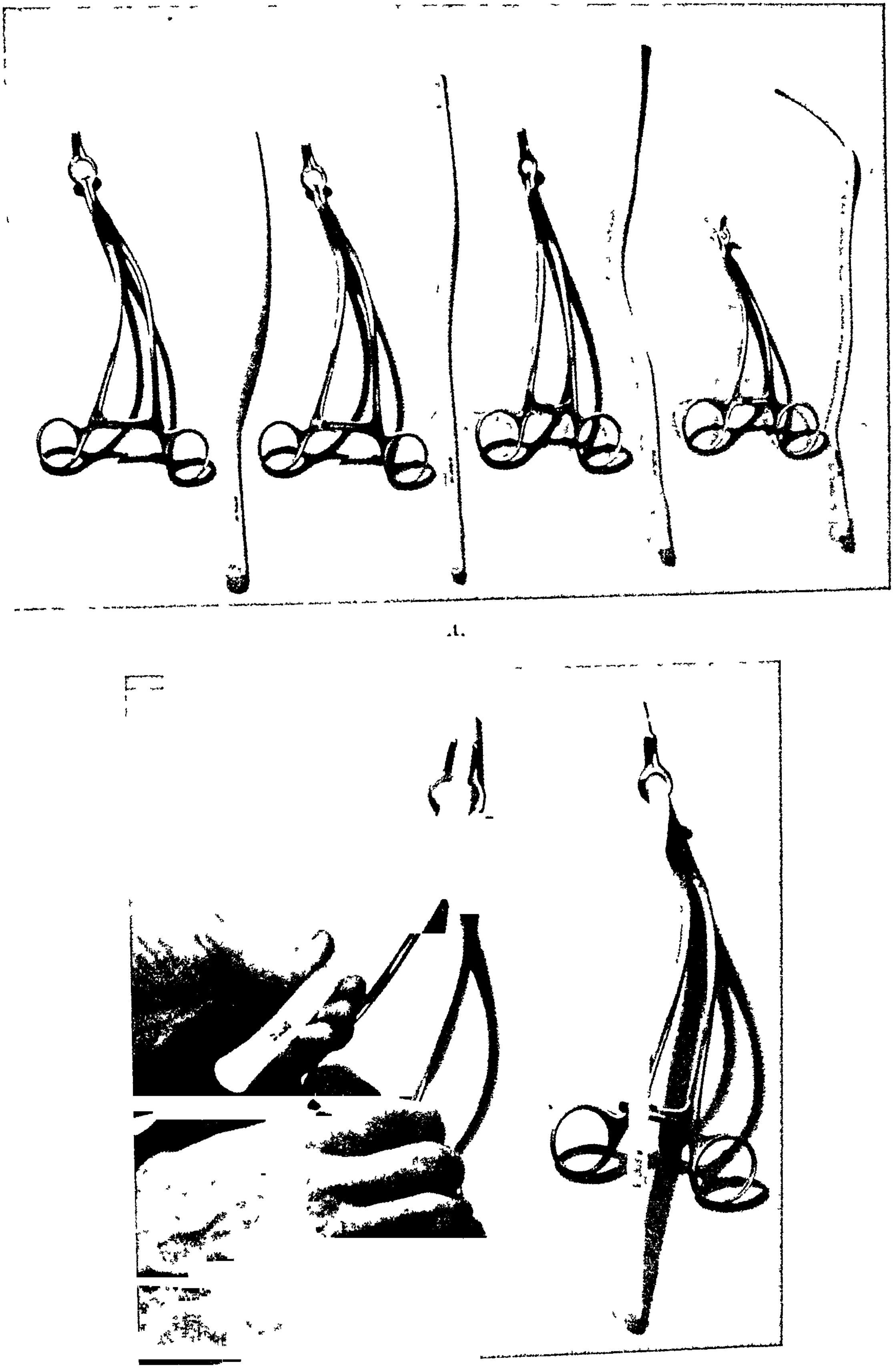

Fig 1—*A*, Photograph showing the four sizes (Nos 40, 30, 24, and 12) of Bardic catheters and the clamps which fit them. *B*, Photograph of technique of application of clamp theter

curved Potts clamp, Beck aortic, or Satinsky clamp is placed on the anterior wall of the aorta to exclude a small area. Then, with a bistoury-type pointed blade (such as Bard-Parker, No. 11), an incision is made in the area excluded to permit the passage of the catheter which has been selected. After the tip of the catheter has been placed in the *small incision, the excluding clamp is* removed, the catheter advanced, and the Nuñez clamp is applied. This holds the catheter firmly in place and prevents leakage of blood (Fig. 2). The whole procedure requires approximately 30 seconds.

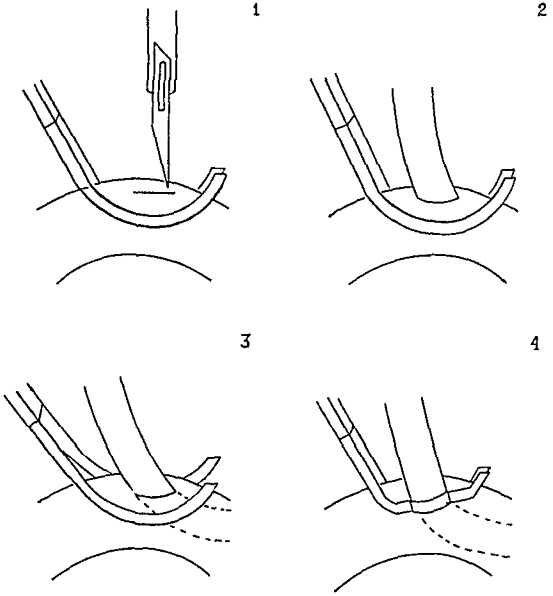

Fig 2.—Diagram of the four steps for inserting the artificial perfusion catheter into the aorta.

At the end of the bypass, the above steps are taken in reverse order. The Nuñez clamp is released slightly and the catheter slipped out until only the tip is inside the aorta. The Satinsky or Potts clamp is applied as the catheter is removed completely, and the aortic incision is sutured.

A description of the first case in which we employed the clamp follows.

CASE REPORT

C. B., a 22-month-old white male, was found to have a heart murmur at 5 weeks of age. Almost since birth it had been noted that he "grunted" at feeding time and after exertion. However, no cyanosis had been present. His mental and physical growth had been slow and on admission he could not sit or stand without assistance.

Physical examination revealed a small but well-developed white infant with no cyanosis or clubbing. He had grunting respiration. There was a moderate increase of the head size and the anterior fontanel was widely open. The lungs were clear. There was a palpable thrill over the third and fourth left anterior interspaces. A blowing systolic murmur (Grade 3) was audible in the same area.

X-ray examination of the heart revealed 2 plus enlargement of the right ventricle and increased vascularity of the lung fields. The electrocardiogram suggested right ventricular hypertrophy. Right heart catheterization revealed data consistent with ventricular septal defect, with pulmonary hypertension. Skull films revealed findings suggesting internal hydrocephalus.

Operation, performed on Aug. 28, 1958, consisted of open ventriculotomy with extracorporeal circulation. Because the femoral arteries were minute in size, the ascending aorta was cannulated with a No. 22 Fr. Bardic catheter, employing the Nuñez clamp as previously described. The venae cavae were cannulated individually through the right atrial appendix. A blood flow of 600 c.c. per minute was easily obtained.

There was a 1 cm. defect in the membranous portion of the intraventricular septum, which was closed with an Ivalon patch. The total bypass time was 34 minutes. The patient withstood the procedure well and was taken to the recovery room in satisfactory postoperative condition.

Since then, this technique of cannulation has become more and more commonly employed at our clinic.

SUMMARY

A new instrument has been devised and employed clinically which allows rapid insertion of a catheter into the thoracic aorta. This clamp has been found valuable in obtaining a high extracorporeal flow rate, particularly in small infants.

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THE FATE OF PERICARDIAL PEDICLE GRAFTS USED IN A FIXED POSITION IN VARIOUS CHAMBERS OF THE DOG HEART

Derward Lepley, Jr., M.D., Paul F. Hausmann, M.D., and*
Wilson Weisel, M.D., Milwaukee, Wis.

Because of its structure, proximity, and ready accessibility, the pericardium has been frequently utilized for experimental repair of various lesions of the heart. In 1952, Bailey[1] used rolled pedicle and "flap like" sheets of pericardium to repair acute interventricular septal defects in dogs which were produced by a closed method. All of these grafts became atrophic thickened cords of fibrous tissue and failed in their purpose.

The same year, Glover[4] reported experimental use of a tubed pedicle of pericardium to close atrial and ventricular septal defects and to augment mitral valve closure in insufficiency. Here, too, grafts placed in the ventricular chambers and septum showed degenerative changes and replacement by fibrous tissue after periods of as long as 16 weeks.

Moore,[6] in 1953, used pericardium as a free graft and as a pedicle to form a sling across the ventricle to correct experimental atrioventricular insufficiency. He noted greater contracture and rigidity in those grafts placed across the left ventricle than in those placed across the right ventricle. He also noted less acellularity and degeneration in the pedicle than in the free grafts.

In 1954, Bailey[2] reported clinical experience in correction of mitral insufficiency by means of pericardial slings extending across the ventricle or used as plicating sutures through the leaflets. Here, too, the results were disappointing because of degeneration and replacement by fibrous tissue with resultant contracture.

In most studies the graft has been placed as a mobile structure in a relatively high pressure chamber. The following study was carried out to determine the fate of pericardial pedicle grafts sewn into acute defects in the septa in high pressure (ventricular), low pressure (auricular) chambers, and in the outflow tract of the right ventricle. The graft and pedicle were threaded through the septum to close the septal defects and all were considered to be in a fixed position.

From the Department of Surgery, Marquette University School of Medicine and Wood Veterans Administration Hospital, Milwaukee, Wis.

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*Presently Research Fellow, National Heart Institute, University of Minnesota.

METHOD AND MATERIALS

Unprepared mongrel dogs were used in all experiments. Sodium Pentothal was used in amounts adequate to maintain light anesthesia. A right thoracotomy was performed and the venae cavae encircled with tapes. A femoral artery was cannulated for arterial return from the extracorporeal circuit. Cannulae draining the venae cavae were brought through the right atrium and connected to a gravity drainage reservoir. Complete heart-lung bypass was carried out by means of a Sigmamotor finger pump, developed at the University of Minnesota, and a plastic sheet oxygenator.* Prior to cannulation, heparin was given intravenously in the amount of 1.5 mg. per kilogram of body weight. Following bypass, protamine was given in a dosage equal to twice that of the heparin administered. At completion of the cardiac operation, the chest was closed and

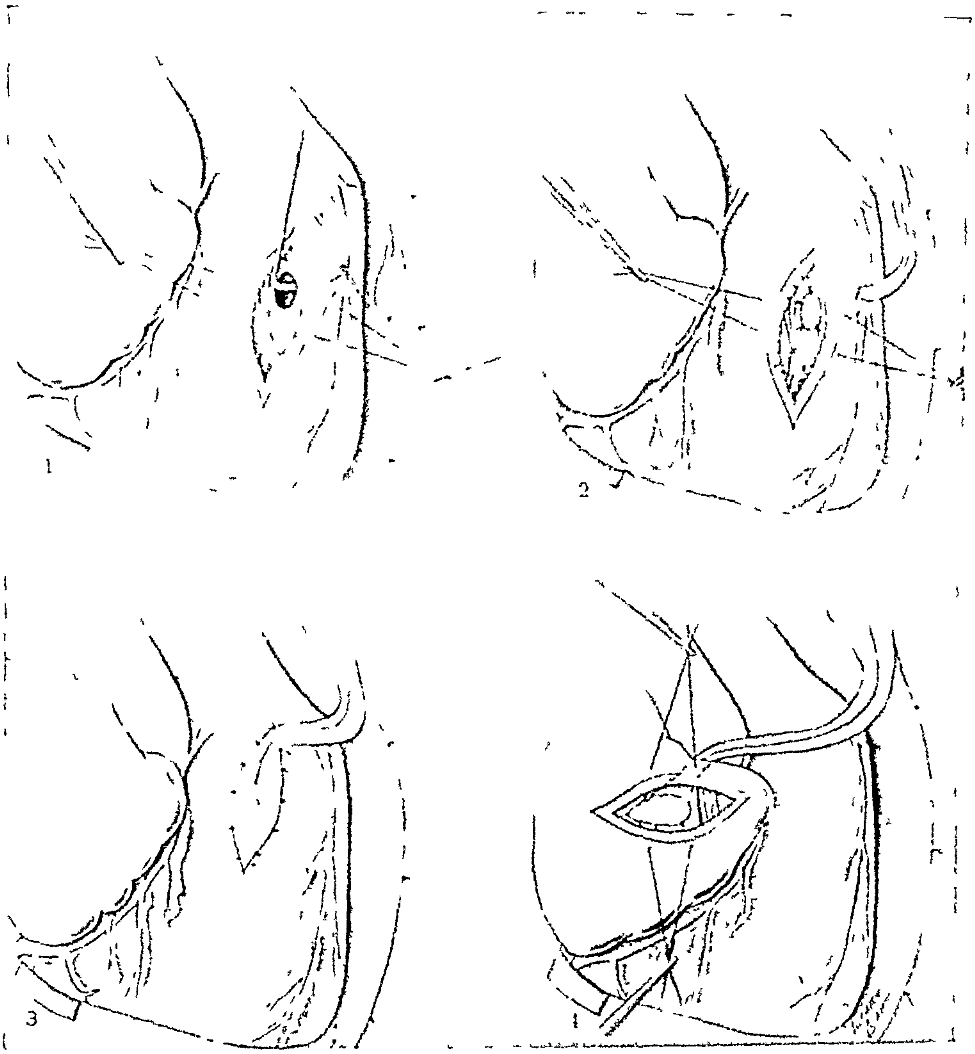

Fig. 1.—Method of placement of pericardial pedicle grafts in each of the three groups of experiments.

1, Pedicled graft picked up by a ligature carrier to be pulled through the ventricular septum. *2*, The graft is sutured in place. *3*, The graft and pedicle are pulled through the interauricular septal plane and sutured into the defect. *4*, The pedicled graft sewn into position in the outflow tract of the right ventricle.

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*Travenol Laboratories, Morton Grove, Ill.

tubes brought out for subaqueous drainage. The tubes were removed after drainage ceased and the lungs were expanded. Three groups of experiments were carried out.

Group I.—A right ventriculotomy was performed and an 11 mm. defect created high in the anterior muscular septum with a cork borer (Fig. 1, *1* and *2*). The previously tailored pedicle of pericardium was pulled through the septum and ventricular wall with a ligature carrier. The pedicle graft was then sutured over the defect with interrupted 4-0 silk sutures and the ventriculotomy closed. It was not necessary to place sutures at the site of entry of the graft in the ventricular wall.

Group II.—A right auriculotomy was performed and a 1 cm. area of the auricular septum was removed. Under direct vision, a ligature carrier was passed through the plane of fusion of the auricular septum and the pedicle graft brought into the defect (Fig. 1, *4*). This graft was then sutured into place with interrupted 4-0 sutures and the auriculotomy closed.

Group III.—A right ventriculotomy was performed and a tailored pedicle of pericardium was used to close the ventriculotomy in the outflow tract. The graft portion was 2 cm. wide and 3 cm. long. Continuous sutures of 4-0 arterial silk were used to suture the graft to the myocardium (Fig. 1, *3*).

All animals that survived were sacrificed 6 months after operation and autopsy was performed. The heart was carefully examined grossly, photographed, placed in formalin, and subsequently sectioned for microscopic study. Sections were cut through the graft site and through the pedicle. These were studied grossly and microscopically using hematoxylin and eosin stains for evidence of survival of the graft, calcium deposition, and degree of circumferential scarring.

RESULTS

Group I.—Twenty-four animals were operated upon and 11 of them survived 6 months. Of the remainder, 6 succumbed on either the day of surgery or the first or second postoperative day due, in most cases, to bleeding or pulmonary complications. Six animals succumbed 3 days to 3 weeks after operation, 3 of empyema and 3 of distemper.

All animals were autopsied and in every instance the defect was completely closed. No evidence of ante mortem thrombus was found in those succumbing early or upon sacrifice. Table I depicts the pertinent gross and microscopic findings in all three groups. It is noteworthy that shrinkage of the graft occurred in about 50 per cent of animals in Group I. In no instance was a smooth flat surface seen either on the right or left ventricular side of the defect (Fig. 2). Calcium deposition was seen grossly in three instances and additionally in three others microscopically.

The pedicle of the graft was identified grossly in 6 and microscopically in 5 of the animals. In the remaining 5, it had become incorporated into the scarred adherent pericardium and could not be identified.

TABLE I. EVALUATION OF GROSS AND MICROSCOPIC APPEARANCE OF THE DEFECT CLOSURE SITE ON SACRIFICING THE ANIMAL 6 MONTHS AFTER OPERATION

EXPER. NO.	SITE OF GRAFT	ORIG. DIAM. DEFECT	GROSS					MICROSCOPIC		
			DIAM. AT AUTOPSY (6 MO.)	SCARRING AROUND MARGINS	DEFECT CLOSED	PEDICLE OF GRAFT IDENTIFIED	CALCIUM DEPOSITED	DEGREE OF SCARRING	VESSELS PATENT	PEDICLE IDENTIFIED
36	Vent. septum	11 mm.	8 mm.	+++*	Yes	No	No	++*	Yes	Yes
38	Vent. septum	11 mm.	6 mm.	+++	Yes	No	Yes	+++	Yes	No
40	Vent. septum	11 mm.	6 mm.	++	Yes	Yes	No	++	Yes	No
46	Vent. septum	11 mm.	6 mm.	+++	Yes	No	No	+++	Yes	No
47	Vent. septum	11 mm.	5 mm.	++	Yes	No	No	+++	Yes	No
50	Vent. septum	11 mm.	6 mm.	+++	Yes	Yes	Yes	+++	Yes	Yes
51	Vent. septum	11 mm.	6 mm.	++	Yes	Yes	No	++	Yes	No
53	Vent. septum	11 mm.	5 mm.	+++	Yes	Yes	Yes	+++	Yes	Yes
54	Vent. septum	11 mm.	6 mm.	+++	Yes	Yes	No	++	Yes	Yes
55	Vent. septum	11 mm.	5 mm.	+++	Yes	No	No	++	Yes	Yes
59	Vent. septum	11 mm.	9 mm.	++	Yes	Yes	No	+++	Yes	No
60	Interatrial septum	1 cm.	8 mm.	+	Yes	Yes	Yes	++	Yes	Yes
64	Interatrial septum	1 cm.	9 mm.	+	Yes	Yes	No	+	Yes	Yes
68	Interatrial septum	1 cm.	1 cm.	+	Yes	Yes	No	+	Yes	Yes
69	Interatrial septum	1 cm.	1 cm.	+	Yes	Yes	No	+	Yes	Yes
71	Interatrial septum	1 cm.	1 cm.	+	Yes	No	No	+	Yes	Yes
73	Interatrial septum	1 cm.	9 mm.	+	Yes	Yes	No	++	Yes	No
76	Interatrial septum	1 cm.	9 mm.	+	Yes	Yes	No	+	Yes	Yes
79	Pulm. outflow tract	3 by 2 cm.	3 cm. by 4 mm.	+++	Yes	No	No	++	Yes	No
81	Pulm. outflow tract	3 by 2 cm.	2 cm. by 6 mm.	+++	Yes	No	No	+++	Yes	No
82	Pulm. outflow tract	3 by 2 cm.	2 cm. by 5 mm.	+++	Yes	No	No	++	Yes	No
84	Pulm. outflow tract	3 by 2 cm.	3 cm. by 6 mm.	+++	Yes	No	No	+++	Yes	No
86	Pulm. outflow tract	3 by 2 cm.	3 cm. by 4 mm.	+++	Yes	No	No	+++	Yes	No

*+ = Mild. ++ = Moderate. +++ = Severe.

Microscopically, there was rather intense fibrous tissue proliferation about the graft extending a variable distance into the myocardium (Fig. 2, *B*). Chronic inflammatory reaction about the silk sutures was pronounced. In the sections through the pedicle within the ventricular wall and septum, the pedicle was seen as a rounded mass of fibrous tissue with little reaction around it, but endothelium could not be identified. In each instance the graft was replaced by a large mass of fibrous connective tissue showing little cellularity and in some instances elevated above the septum 3 to 6 mm. Thrombosed vessels were not seen in any of the sections.

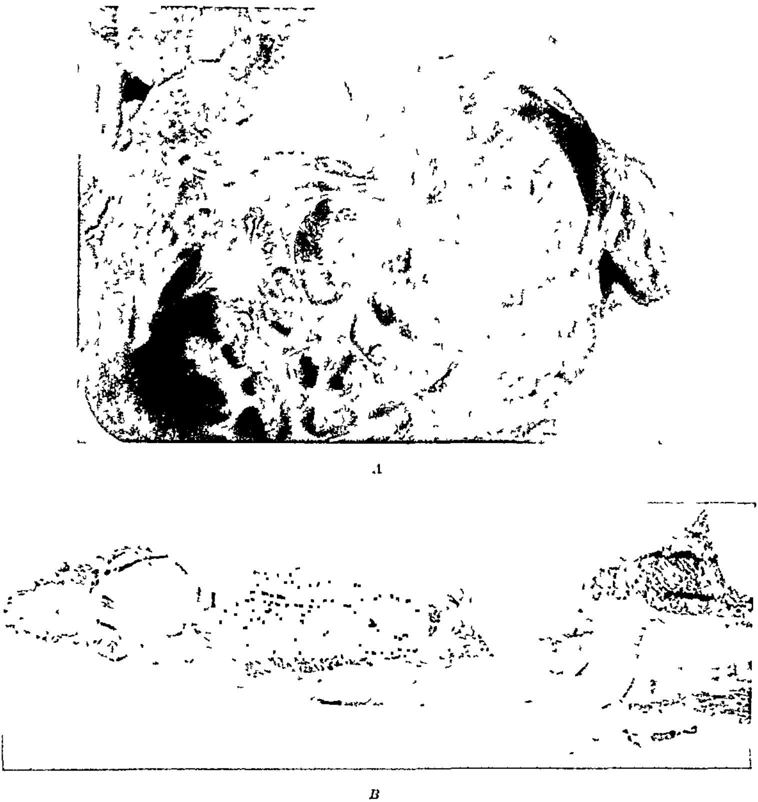

Fig 2.—Heart of Dog No 59 sacrificed 6 months after placing a pedicled pericardial graft in ventricular septal defect.

A, The right ventricle is opened The septal defect in the center is healed and a mound of contracted fibrous connective tissue has replaced the graft. The healed ventriculotomy is at left.

B, Photomicrograph showing the healed defect in cross section.

Group II.—Auricular septal defects were made in 13 animals and were closed with pericardial pedicle grafts. Of these, 7 survived 6 months and were sacrificed for study. The remainder died from one day to 3 weeks following operation from the effects of surgical heart block, bleeding, or from infection.

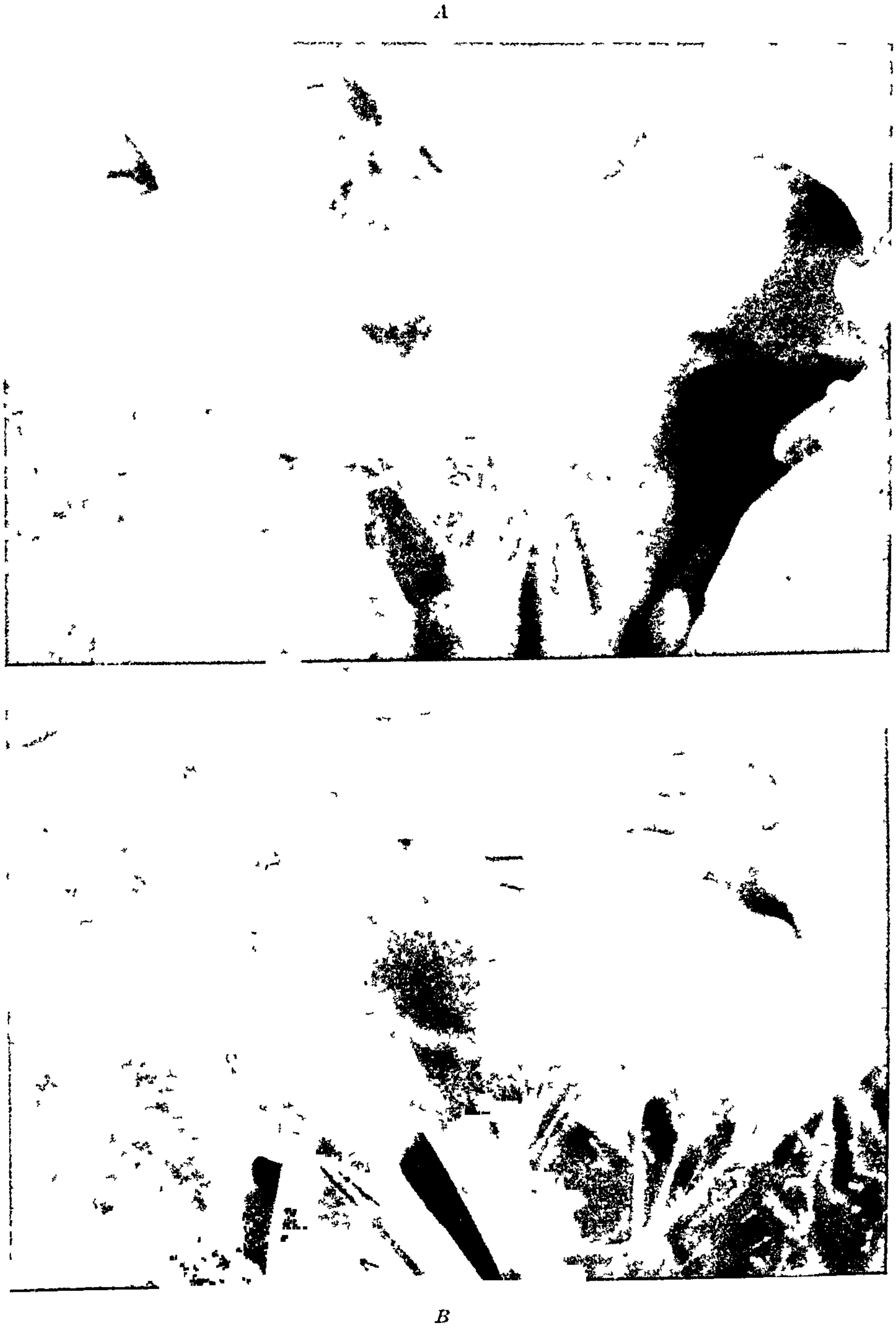

Fig. 3.—Heart of Dog No. 73. Atrial septal defect closed with pedicled pericardial graft. Sacrificed after 6 months.

A, Right atrial septum. The defect is well healed and scarring at the margins is not marked.

B, Left auricular septum.

In all animals, the defects were found to be closed at the time of death. On gross examination, marginal scarring and shrinkage of the graft were found to be minimal in the 7 surviving 6 months (Fig. 3). In 4 of the 7, the graft and its margins were soft and pliable The other 3 presented some rigidity and thickening on palpation. In all but one, the graft pedicle was easily found in the interauricular plane. Microscopically, the graft showed a normal cellularity except for moderate infiltration with fibroblasts and collagen deposition with minimal adjacent scarring as compared to those placed in the ventricular septum. In one instance, calcium deposition was seen and in another there was moderate scarring which appeared to be related to use of too many silk sutures. The pedicle was identified in the septal plane in all but one dog.

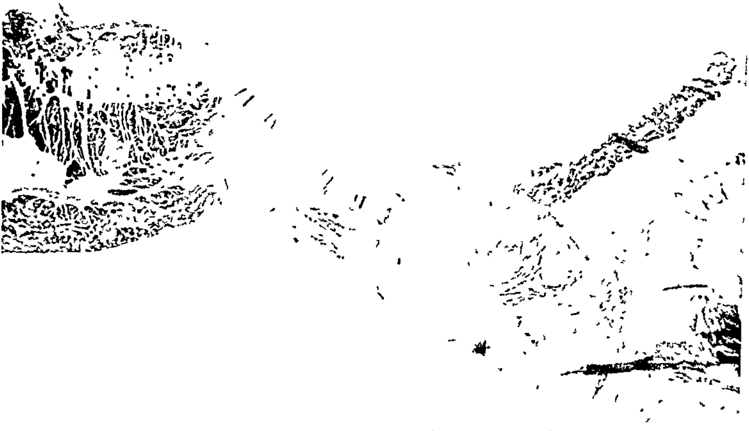

Fig 3.—Cont'd. *C*, Photomicrograph showing a cross section of the graft and pedicle The pedicle is the white mass of fibrous tissue extending away from the defect in the upper left corner

Group III.—A pericardial pedicle graft was placed in the wall of the outflow tract of the right ventricle in 10 animals. Five survived 6 months and were sacrificed for study. The other 5 animals bled to death because of the technical difficulty of obtaining adequate closure between the myocardium and the relatively fragile dog pericardium.

In all surviving animals, shrinkage of the graft was marked, particularly in the lateral plane. The graft was found to be a thickened cord reduced from an original 2 cm. to about 0.5 cm. In no instance was aneurysmal dilatation seen. The pedicle of the graft could not be traced grossly nor microscopically in any of the 5 animals (Fig. 4). Cross sections of the grafts revealed dense acellular fibrous tissue which separated the myocardial edges only 4 to 6 mm. as was noted grossly.

DISCUSSION

The fate of pericardial pedicle grafts in a "fixed" position as opposed to mobile grafts (such as transventricular slings) is determined to large extent by the pressures in the chambers in which they are placed.

Minimal fibrous tissue reaction with resultant scarring contracture was seen in those grafts placed in the auricular septum, whereas marked scarring resulted with the grafts placed in the ventricular chambers. These findings closely correlate with the evidence supplied by other workers.

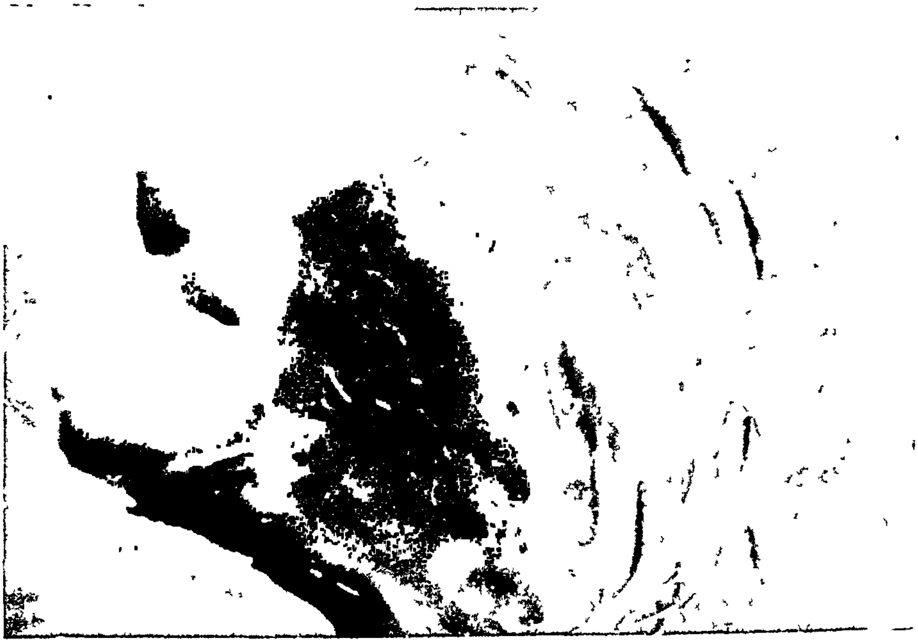

Fig. 1.—Heart of Dog No. 82 showing the fibrous tissue replacement of a graft, 2 cm wide by 3 cm. long, used to bridge the outflow tract of the right ventricle. The animal was sacrificed 6 months after operation

It seems possible that any tissue placed in such a position under a pressure higher than its capillary pressure would be deprived of arterial supply and venous drainage, and could be expected to degenerate with consequent replacement by fibrous connective tissue.

As a result of these studies, it is concluded that a pedicle pericardial graft would be a reasonable prosthesis for use in closure of interauricular defects in human subjects.

SUMMARY

1. Pedicle pericardial grafts were used to close auricular and ventricular septal defects and to enlarge the outflow tract of the right ventricle in dogs.

2. Grafts in the ventricular septum and in the outflow tract of the right ventricle showed marked tissue reaction, degeneration, and were replaced with avascular connective tissue after 6 months.

3. Similar grafts placed in the auricular septum survived without contracture, and fibrous tissue reaction was minimal after 6 months.

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CARDIAC TAMPONADE AS A COMPLICATION OF LEFT HEART CATHETERIZATION

Kamta P. Sinha, M.D., and Edward A. Fitch, M.D.,***
Philadelphia, Pa.

In a recent report, Kavanagh-Gray and Drake[1] reviewed the complications of left heart catheterization. Seven deaths were reported in a series of 490 cases. One death was due to cardiac tamponade as a result of inadvertent puncture and tear of the ascending aorta.[2] Three more cases of cardiac tamponade were reported; however, the exact cause of tamponade was not mentioned. We are reporting 2 cases of massive cardiac tamponade as a complication of left heart catheterization presenting some very unusual features.

CASE REPORTS

CASE 1.—E. G., a 24-year-old white man, entered the Hahnemann Hospital on Aug. 12, 1958. His only complaint on admission was progressive fatigability on moderate to mild exertion. He denied having dyspnea, orthopnea, palpitation, cough or hemoptysis. He did not remember having rheumatic fever or its equivalent. A heart murmur was first discovered in a routine school examination at the age of 13. He did not develop any symptoms until 6 months previously when he noticed that he was easily tired on his usual job. The past history and family history were noncontributory except for complete paralysis of the left facial nerve since birth.

Physical examination revealed a young healthy male in no obvious discomfort. Pulse rate was 100 per minute and regular. Blood pressure was 130/60 mm. Hg. Head and neck were not remarkable except for the incidental finding of the paralysis of the left facial nerve. The lungs were clear on auscultation. There was a palpable diastolic thrill at the mitral area. The apical impulse was not forceful. Auscultation at the apex revealed a sharp mitral first sound, no systolic murmur, opening snap, and Grade 2 mid-late diastolic rumble. Pulmonic second sound was louder than aortic. There was also a Grade 1 early diastolic murmur at the third intercostal space at the left sternal border. Examination of the abdomen and extremities was negative. Peripheral signs of aortic regurgitation were not present.

Radiologic examination revealed a normal-sized heart with minimal enlargement of the left atrium (Fig. 1). There was suggestive evidence of left ventricular strain and hypertrophy on the electrocardiogram (Fig. 2). A tentative diagnosis of mitral stenosis due to rheumatic heart disease was made. However, aortic valve disease could not be ruled out. Suprasternal transthoracic aortography was performed according to the technique of Lehman, Lemmon,

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*Research Fellow in Cardiology, Brith Sholm Cardiopulmonary Laboratory, and Hahnemann Medical College and Hospital, Philadelphia, Pa.

**Public Health Service Research Fellow of the National Heart Institute; Resident in Thoracic Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pa.

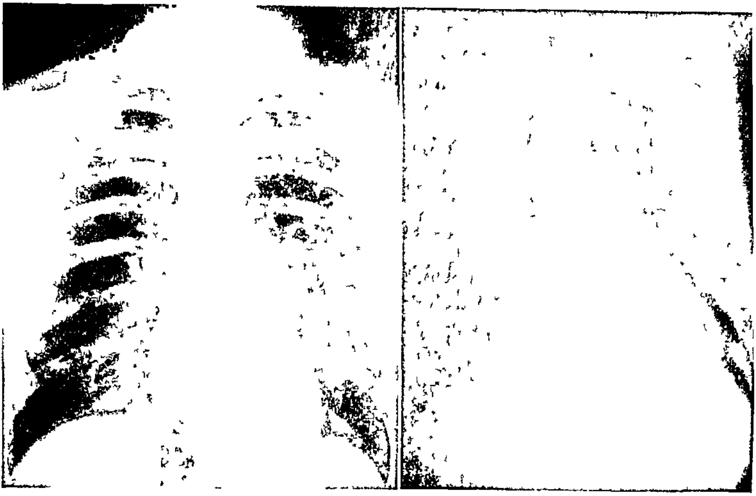

Fig 1—Posteroanterior and right anterior oblique views of chest showing normal-sized heart and minimal enlargement of left atrium

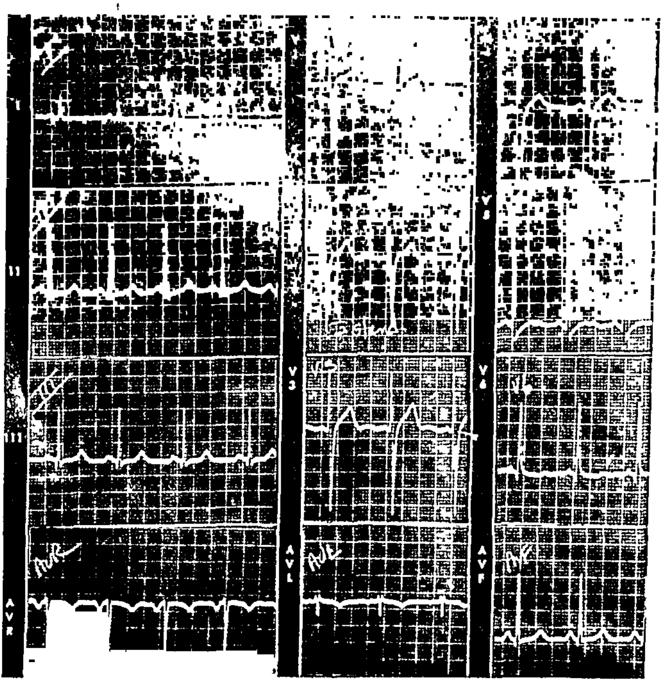

Fig. 2—Electrocardiogram of the patient with suggestive evidence of left and hypertrophy.

Boyer, and Fitch.[3] Aortic regurgitation was thereby ruled out. However, the morphology of the aortic valvular region was abnormal and suggested the presence of a bicuspid valve (Fig. 3).

A left heart catheterization with dye studies was planned to determine the severity of altered hemodynamics due to mitral stenosis and also to rule out aortic stenosis. The left heart catheterization was started according to the usual technique with a premedication of Seconal, 1½ grains, and Demerol, 50 mg. During the first two attempts the needle did not enter the left atrium; however, during the third attempt the needle entered a chamber which was thought to be the left atrium inasmuch as bright red blood came out of the needle at very low pressure. In addition, several atrial premature beats were noted on the electrocardiogram at the time of the needle puncture. At this time, the patient suddenly developed a marked bradycardia of 16 beats per minute followed by a generalized convulsive seizure. The needle was immediately withdrawn from the back and 1 c.c. of atropine was given intramuscularly. An endotracheal tube was introduced and oxygen insufflation started. For a moment the bradycardia improved and the cardiac rate increased to 100 beats per minute. The blood pressure was unobtainable, although a carotid pulse was palpable. In a few moments marked bradycardia again occurred with a bizarre ventricular complex. Heart sounds could not be heard. The carotid pulse faded beneath the palpating finger to become imperceptible in a few seconds. This pathognomonic evidence of failing cardiac action prompted an immediate left anterior thoracotomy. There was massive hemopericardium present, resulting in cardiac tamponade. The heart had stopped. The pericardium was incised anterior to the phrenic nerve and the tamponade relieved. An estimated 500 c.c. of blood gushed from the pericardial sac. The heart was small and flabby. Cardiac massage was instituted as the feet were raised high to provide a venous autotransfusion. Unmatched type O blood was obtained promptly from the blood bank and pumped into a peripheral vein. Still

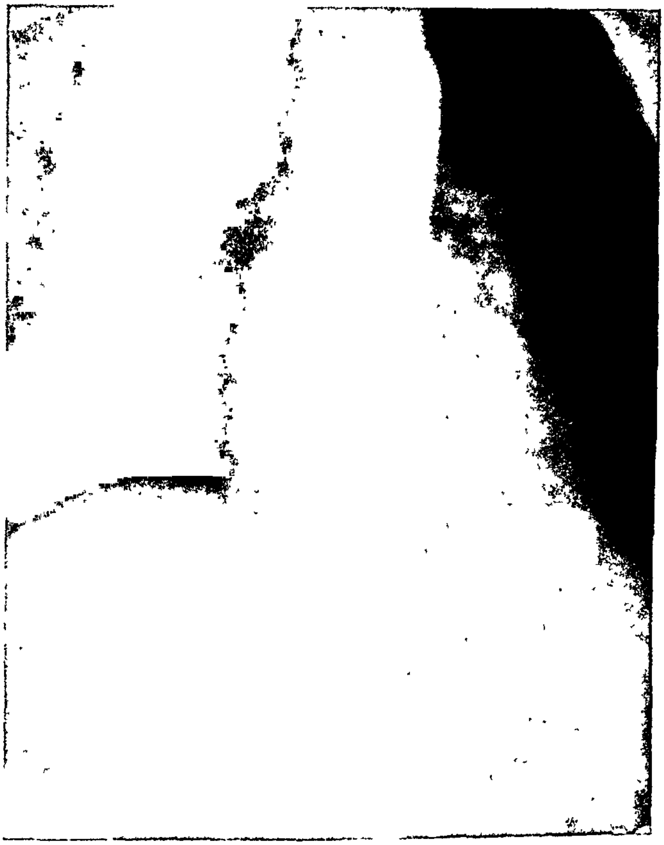

Fig. 3.—Aortogram of the patient showing slight deformity of the aortic valves without any aortic regurgitation.

cardiac contractions were feeble and ineffective, although increased ventricular filling was evident under the massaging hand. One cubic centimeter of 1:1000 Adrenalin was injected into the left ventricular cavity. Prompt and effective contractions ensued. The blood pressure was still very low (Fig. 4). At this stage, it was noted that there was a continuous oozing of blood. The source of bleeding could not be ascertained. The patient was put on Bennett's respirator and a transternal bilateral thoracotomy completed. The heart was lifted to visualize the posterior surface of the left atrium No bleeding was found. A jet of blood spurting from the coronary aortic sinus was located by the exploring finger. The rent seemed to be about 0.5 cm. in length and located in the thinnest portion of the wall of the ascending aorta, i.e., the aortic sinus. The tear was sealed with the finger while the heart rate and blood pressure stabilized (Fig. 5). Nine pints of blood were infused. The rent was sutured and the chest closed. The entire procedure was performed on the cardiac catheterization table and was completely unsterile.

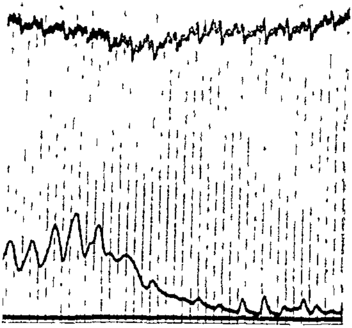

Fig 4.—Brachial artery pressure tracing showing very low arterial pressure before the suture of the tear in the aorta.

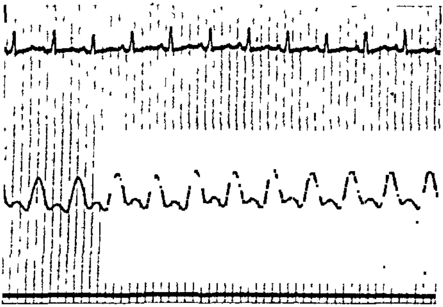

Fig. 5—Brachial artery pressure tracing showing the established arterial pressure after the suture of the tear in the aorta.

A tracheotomy was performed for retained secretions. Heavy doses of multiantibiotic therapy were used. The first 3 days were stormy; complicated by pneumonitis, retained secretion, mental confusion, hyperpyrexia, myocardial irritability (Fig. 6), and electrolyte imbalance. However, the rest of the hospital course was uneventful.

Case 2.—J. B., a 43-year old white woman, entered the Hahnemann Hospital on Aug. 8, 1958. The patient was in good health until 18 months previously, when she had suddenly vomited a large quantity of blood. At that time a heart murmur was discovered and the patient was told that she had heart disease. From that time on the patient gradually developed weakness and exertional dyspnea. However, she never experienced any orthopnea or palpation. Fluid began collecting all over her body, starting from the lower extremities. She was put on digitalis and diuretics. At the time of the present admission to the hospital her chief complaints were swelling of abdomen and extremities, generalized weakness, and easy fatigability. The patient denied having rheumatic fever or its equivalent. The rest of the history was noncontributory.

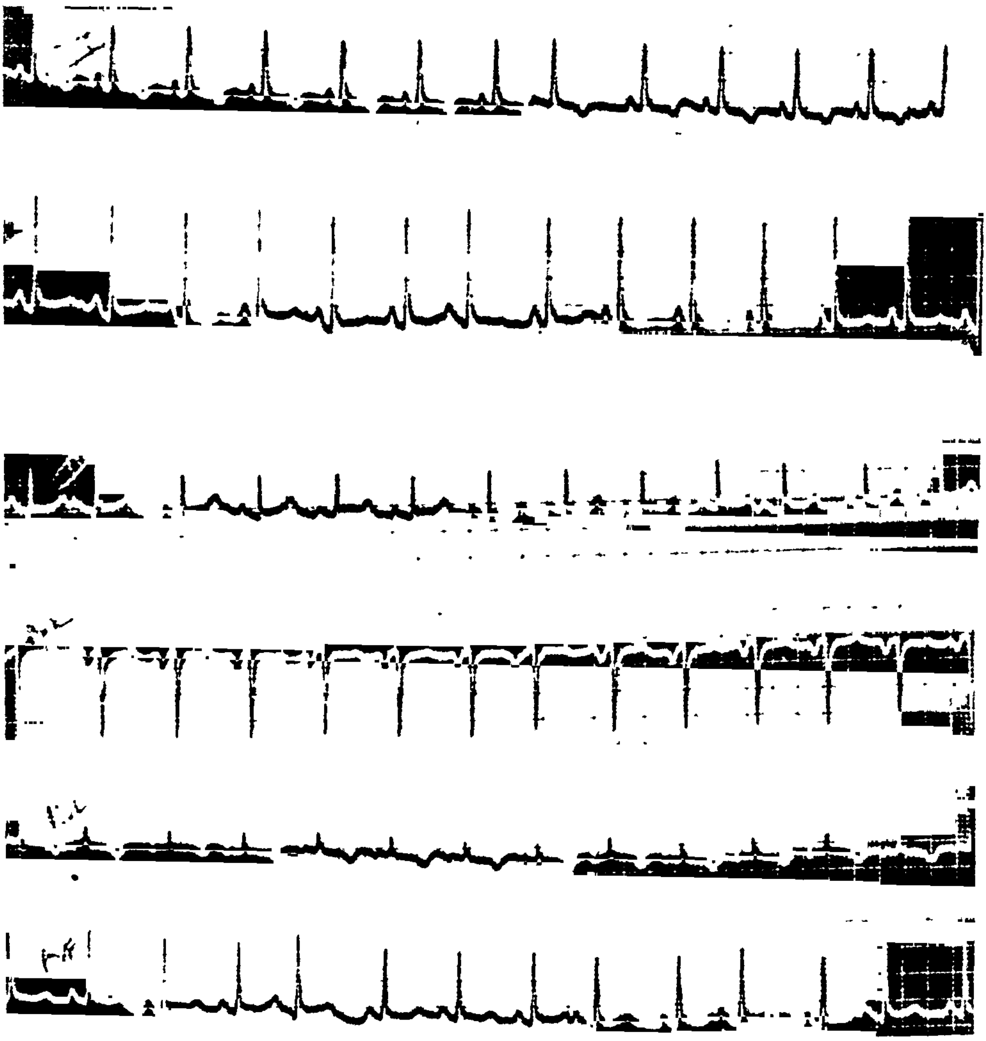

Fig. 6.—Postoperative electrocardiogram showing change in aV_L.

Physical examination revealed a chronically ill female with marked ascites and swollen extremities. Pulse rate was 84 per minute and regular. Blood pressure was 100/60 mm. Hg. Neck veins were prominent and pulsating. There was some facial edema. Auscultation of lungs revealed bilateral râles, but there was no evidence of pleural effusion. Apical impulse was displaced to the left and there was also a palpable impulse at the fourth left interspace at the side of the sternum. On auscultation there was a blowing systolic murmur of Grade 2 to Grade 3 intensity at the mitral area. Mitral first sound was loud. There was no diastolic murmur. Pulmonic second sound was 2 to 3 plus accentuated. Examination of the abdomen revealed 3 plus ascites. Liver could not be palpated due to the massive ascites. There was 2 to 3 plus edema of the extremities.

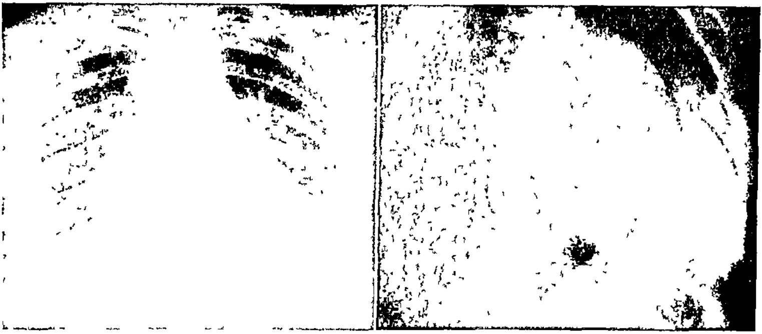

Fig. 7.—Radiogram of the Patient J. B showing marked enlargement of the heart size

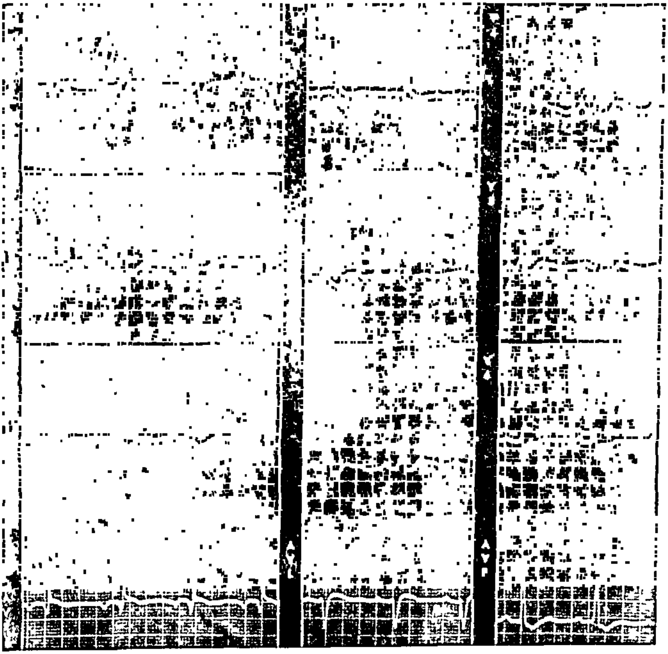

Fig. 8.—Electrocardiogram of the Patient J. B. showing evidence of right ventricular hypertrophy.

Laboratory investigations revealed some evidence of renal and hepatic damage as indicated by 23 per cent excretion of the dye at the end of 2 hours in phenolsulfonphthalein test and retention of 28.4 per cent of the dye at the end of 45 min. in Bromsulphalein test. However, in the presence of marked congestive failure, these values could not be properly interpreted. A Congo-red test was done showing the disappearance of only 15 per cent of the dye. Serum iron was 76 mg. per cent (normal range is 50 to 180 mg. per cent).

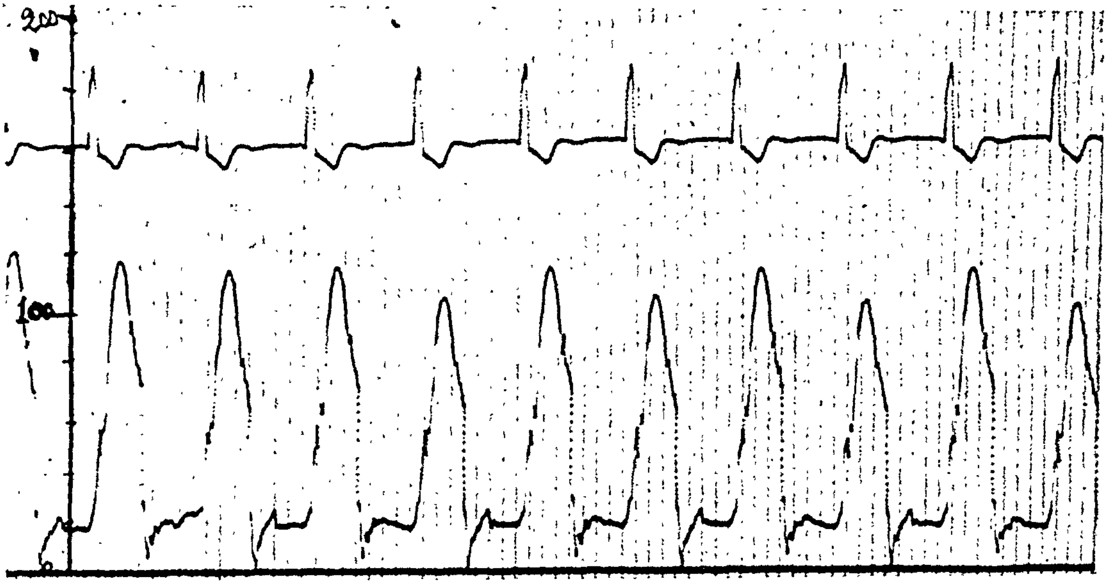

Fig. 9.—Pressure tracing of the right ventricle showing a sudden rise in diastolic pressure after an initial drop. (Commonly seen in constrictive pericarditis and failing myocardium.)

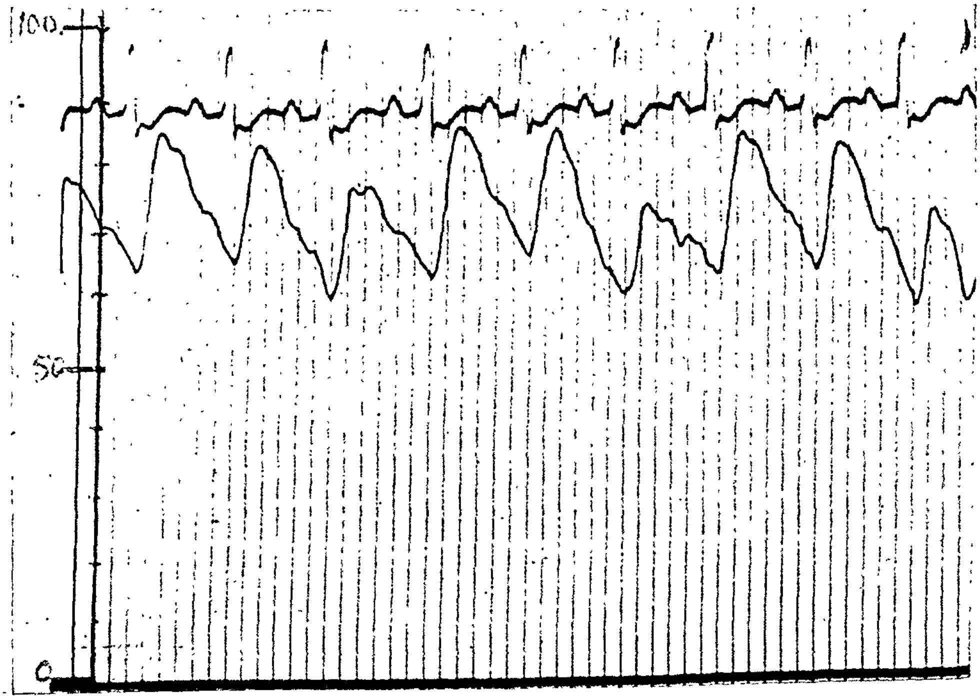

Fig. 10.—Pressure tracing, showing that the needle entered a high pressure vascular chamber (aorta).

Venous pressure in the basilic vein was 130 mm H_2O and on abdominal compression it rose to 370 mm H_2O. Arm to tongue circulation time was 30 seconds and arm to lung was 6 seconds.

Radiologic examination revealed the size of the heart to be 3 plus enlarged. The enlargement of the specific chamber could not be accurately defined. The pulmonary artery segment and hilar vessels were 2 to 3 plus enlarged. There was no evidence of classification either in the pericardium or at the valve area (Fig. 7). A contrast x-ray study of the esophagus and upper gastrointestinal tract was normal.

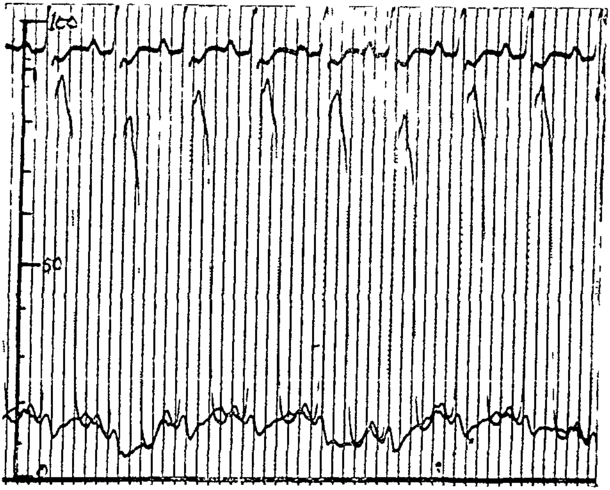

Fig. 11.—Pressure tracing of left ventricle and left atrium taken simultaneously. There is no evidence of mitral stenosis.

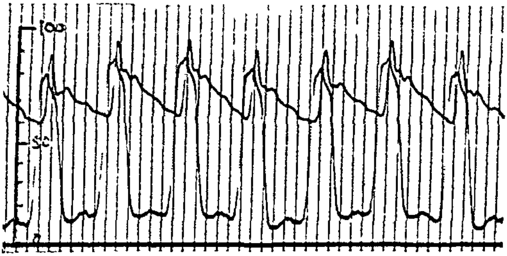

Fig. 12.—Pressure tracing of left ventricle and brachial artery taken simultaneously. There is no evidence of aortic stenosis.

There was evidence of right ventricular hypertrophy in the electrocardiogram (Fig. 8).

At this stage a definitive diagnosis could not be made. The following possibilities were considered: (1) mitral stenosis with tricuspid insufficiency, (2) constrictive pericarditis, and (3) essential pulmonary hypertension. A right and left heart catheterization was contemplated to reach a more definitive diagnosis.

On right heart catheterization, the pressure in the right ventricle and pulmonary artery was greatly elevated (R. V. 122/19) with a deformity of the pressure tracing during the diastole of the right ventricle (Fig. 9). There was no evidence of intracardiac shunt. A left heart catheterization was then attempted. The needle went into the aorta (Fig. 10). The needle was then withdrawn and in the second attempt it entered the left atrium and then to the left ventricle. All the pressures were obtained. It did not show any gradient across the mitral or the aortic valve (Figs. 11 and 12). Apparently the patient was in good condition and was sent back to her room. In the evening, at 7 P.M., the patient suddenly collapsed and there was no pulse. Hand bellows respiration and pericardial paracentesis were immediately performed. Blood escaped under pressure and a total of about 400 c.c. of blood was withdrawn. At the end of the procedure, the blood pressure rose to 96/60 mm. Hg. At about 4 A.M., the patient again had a similar attack. Again a needle was introduced in the pericardium but nothing came out. As the needle was withdrawn, the patient developed cardiac arrest. The chest was opened. There was about 200 to 300 c.c. of blood and blood clots in the pericardium. It was removed and cardiac massage was started. For a while the heart seemed to come back to normal sinus rhythm, but again it stopped. The patient was pronounced dead. There was no evidence of constrictive pericarditis. Multiple strips from lung and atrium were taken for biopsy studies. Histology examination of the atrium was normal except for some hypertrophy of the muscular layer. There was no evidence of fibroelastosis. Microscopic examination of the lung showed moderate thickening of the layer of pulmonary arteries due to medial hypertrophy. There was occasional subintimal proliferation. Arterioles showed areas of fibrosis (Fig. 13). These findings were consistent with pulmonary hypertensive disease.

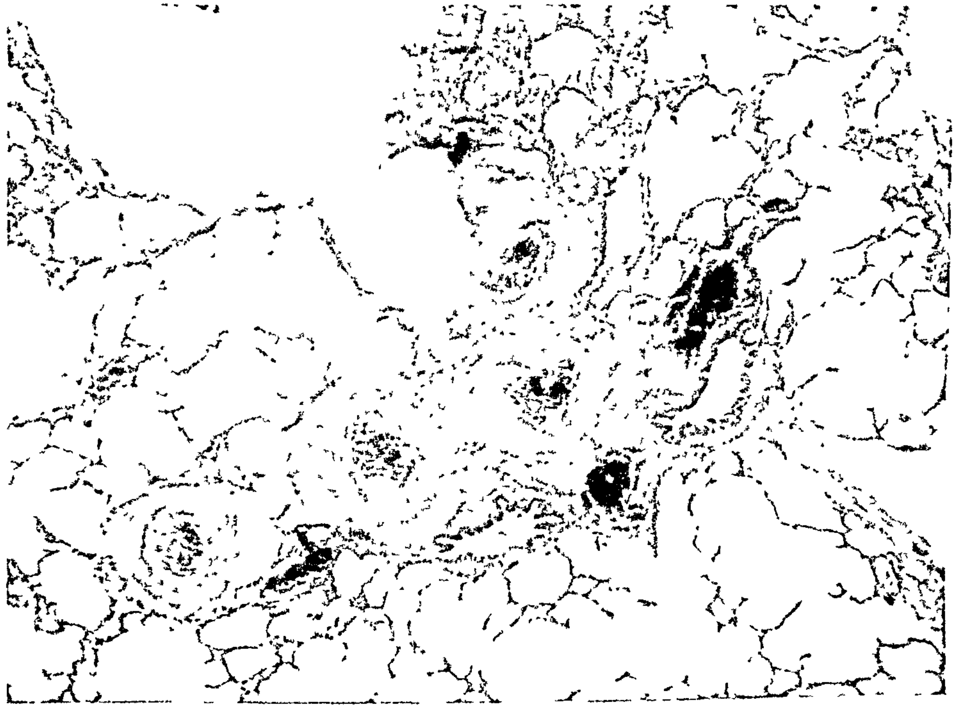

Fig. 13.—Microphotograph of the biopsy of lung showing medial hypertrophy and subintimal proliferation of the branches of pulmonary artery. Arterioles show areas of fibrosis.

DISCUSSION

Left heart catheterization is a routine procedure in cardiac centers interested in the detailed study of cardiopulmonary pathophysiology. However, there is no uniformity with regard to the technique of left heart catheterization. In our experience, Fisher's modification of Bjork's procedure has been most satisfactory. However, in aortic valve disease and in cases of mitral valve disease with normal sized left atrium, the puncture of the aorta is not uncommon. Similar experiences have been reported by most of the cardiologists who use this technique.[2,4,5] Bagger, Bjork, and Malonstrour's patient died of cardiac tamponade due to puncture of the ascending aorta.[2] However, they felt that a prompt surgical intervention might have saved the patient. A British group led by Sir Russel Brock[4] had 3 deaths in a series of 24 cases. He emphasized the complication of puncturing the aorta in cases of normal sized left atrium, so much so, that he does not employ this procedure in aortic valve disease. In such cases, he punctures the left ventricle directly from the anterior approach and measures the LV BA gradient by putting a Cournand needle in the brachial artery. In our experience, puncture of the aorta is infrequent and complications due to this are very uncommon. On the other hand, in transthoracic suprasternal aortography, the aorta is entered at its root with a needle identical in size to that of the left heart catheterization needle, usually in the extrapericardial thicker portion of the aortic wall.

In our first case, the puncture of the aorta was followed by a tear of its wall resulting in cardiac tamponade. This is the second case in literature in which cardiac tamponade developed due to a tear of the aorta. Bjork's patient died. Due to prompt surgical action taken by the surgical team present our patient recovered. In our second case, cardiac tamponade developed gradually and thoracotomy failed to help the patient.

SUMMARY

Two cases of massive cardiac tamponade, one due to a tear of the root of the aorta and the other due to puncture of the aorta during left heart catheterization, are reported. The inherent danger of unintentional aortic puncture during left heart catheterization in cases of normal sized left atrium is emphasized. The prompt surgical action to relieve the tamponade and suture the aortic tear was lifesaving in our first case.

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PRIMARY MEDIASTINAL TUMORS

Joseph Hodge, M.D., Gonzales Aponte, M.D., and*
Edward McLaughlin, M.D., Philadelphia, Pa.

THERE have been many reports concerned with the classification, description, and treatment of mediastinal tumors and cysts. This paper is a review of a series of 42 unselected cases of primary mediastinal tumors originating in the mediastinum and classified on the basis of pathologic types in specific anatomic locations. The large number of thymomas in this relatively small series is noteworthy.

DATA AND METHOD

During the years 1942-1958 inclusive, 74 cases diagnosed as being mediastinal neoplasms were found in the clinical and necropsy records of the Departments of Surgery and Oncology of the Jefferson Medical College Hospital. Forty-two of these were diagnosed as primary mediastinal tumors. Mediastinal masses which did not originate primarily within the confines of the mediastinum per se were excluded from this series. The clinical records have been reviewed and the histologic type of tumor confirmed in each case. These tumors have been divided into benign and malignant thymomas, neurogenic tumors, teratomas and dermoid cysts, and incidental tumors, i.e., bronchial and pericardial cysts, hamartomas, and lipomas. Each type is discussed separately (Table I).

INCIDENCE

Neurogenic neoplasms, benign and malignant, are the most common types encountered in the series reported by Blades,[1] Brewer,[2] Shidler and Holman,[3] and Ringertz.[4] In this series, neurogenic tumors comprised 26 per cent of 42 primary cases. Malignant and benign thymomas comprised the most frequent tumor, 43 per cent of the total, as compared to 7.5 per cent thymomas of a total of 241 mediastinal tumors reported by others.[1-6] Ringertz and Lidholm found thymoma present in 19 of 155 cases (12 per cent) of primary and secondary mediastinal neoplasms studied. Six different reports ranked teratoid tumors and cysts second in frequency.[1-6] This variety was third in our series and accounted for 19.0 per cent of the cases. The remainder of our cases consisted of pericardial and bronchial cysts, intrathoracic lipoma, and hamartoma.

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*Present address: Hodge Clinic, 3 Catawba Street, Spartanburg, S. C.

TABLE I. M[illegible] TUMORS

			PER CENT OF TOTAL OF NEOPLASMS REPORTED
Thymomas			
Benign	4		
Malignant	14		
			42.9
Neurogenic Tumors			
Benign	10		
Malignant	1		
			26.2
Teratomas and Dermoid Cysts			
Benign (2 each)	4		
Malignant (2 each)	4		
			19.0
Incidental Tumors			
Bronchial cysts	2		
Hamartomas	1		
Lipomas	1		
Pericardial cysts	1		
			11.9
Total Number of Neoplasms Reported		42	100

THYMOMA

Thymoma was the type of mediastinal neoplasm encountered most frequently in this study. The average age of the patient was 41.2 years and it occurred more commonly in males of the white race (Table IIB).

The most common site in our series was the upper anterior mediastinum. The tumor may also be found in the superior or middle mediastinum or other locations.[8]

Dyspnea and cough were the chief complaints in over 64 per cent of the patients. Chest pain was a complaint in 55 per cent of the malignant group. Symptoms of myasthenia gravis and cough were present in 2 cases of benign thymoma. Benign thymomas cause symptoms by compression whereas the malignant thymoma invades surrounding structures, i.e., visceral pleura, pericardium, etc. Roentgenograms were diagnostic in approximately 40 per cent of the patients. Three patients were asymptomatic and an intrathoracic mass was discovered by routine x-ray studies. The finding of a quadrilateral form of neoplasm in the anterior mediastinum or superior mediastinum is suggestive of thymoma. Surgical excision was the treatment of choice (Table IIB).

Median sternotomy was the approach utilized in 4 patients. This approach has the advantage of making the gland readily accessible since the mediastinum [illegible] explored from the neck to the diaphragm. Hyperplasia or persistent t[illegible] may be associated with Graves' disease, Addison's disease, and o[illegible]s. The malignant thymomas most frequently observed were [illegible] origin, namely, lymphoepitheliomatous in type (see Fig. 2, A [illegible]). This consisted of an admixture of both lymphocytes and epithelial [illegible] was more common in the adult patients. Other varieties included the lymphosarcomatous, carcinomatous, reticulum and Hodgkin's cell types (see Fig. 2, D and E).

TABLE IIA. INCIDENCE OF THYMIC TUMORS IN SEVERAL SERIES

	HODGE ET AL.	BLADES[1]	BREWER & DOLLY[2]	SHIDLER & HOLMAN[3]	RINGERTZ & LINDHOLM[4]	BRADFORD ET AL.[5]	EFFLER & MC-CORMACK[6]	CURRERI & GALE[7]
Benign thymomas	4	6	2	4	19	3	19	2
Malignant thymomas	14	-	-	-	-	-	-	-

TABLE IIB. THYMOMAS

Total Number of Cases	18	
Age		
6 months to 72 years		
Sex		
10 males—8 females		
Race		
12 white—6 Negro		
Diagnosis		
Benign thymoma—4		
Malignant thymoma—14		
Pathologic Types of Malignant Thymoma Confirmed by Histologic Study of Specimen		
1. Lymphocytic-lymphoepithelioma		7
2. Reticulum cell		1
3. Carcinoma		
Anaplastic primitive epithelioma		1
Lowenhaupt group 1		2
Hassall's corpuscle		1
4. Hodgkin's granuloma		1
5. Lymphosarcoma		1
Associated Disease		
Myasthenia gravis associated with 2 cases of benign thymoma and lymphosarcoma type of malignant thymoma		
Treatment		
1. Operative		
Thoracotomy and excision		14
Thoracotomy and incisional biopsy		1
Supraclavicular node excisional biopsy		1
2. Nonoperative		
Both cases confirmed by autopsy		2

Malignant thymomas metastasize chiefly by direct extension and lymphatic permeation that may involve distal structures of the mediastinum.

Prognosis.—Over 50 per cent of the cases have been followed. Survival ranged from 10 months to 13 years; the average was 3.7 years. Three patients who received radiation in addition to surgical therapy, survived 10 months, 2½ years, and 3 years, respectively.

THYMOMA-MYASTHENIA GRAVIS

Approximately 15 per cent of patients with myasthenia gravis have an associated tumor.[9] Surgical removal of benign thymoma benefits 50 to 70 per cent of the patients[10] and is advisable because of the possibility of malignant transformation.[11, 12, 13] In our series there were 2 benign and 1 malignant thymomas and there were certain common features in each case. The patients presented symptoms of myasthenia gravis (weakness, fatigue, eye signs, ptosis, blurred vision, dysphagia) and pulmonary symptoms, i.e., chest

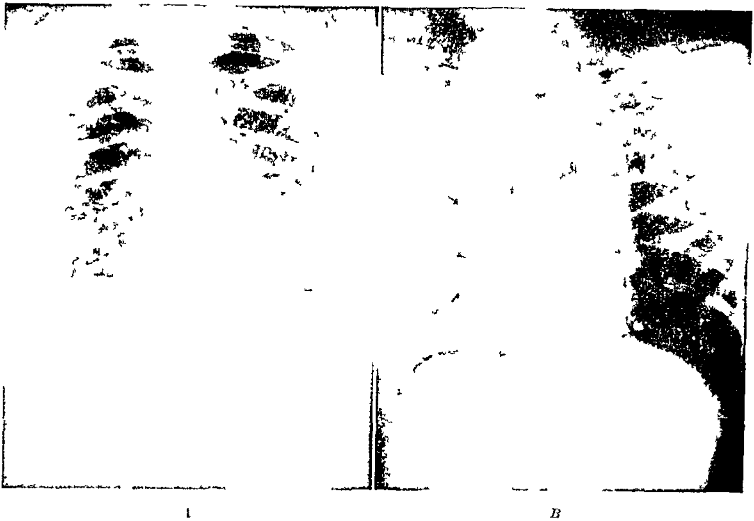


Fig 1 —Malignant thymoma lymphosarcoma Thymoma associated with myasthenia gravis *A*, Chest x ray film—posteroanterior *B* Chest x ray film—lateral

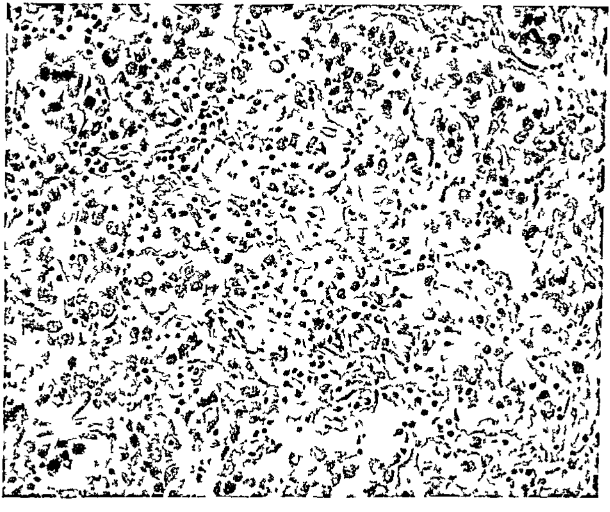


Fig 1 —Cont d *C*, Microscopic section of malignant thymoma A poorly differentiated neoplasm composed of vari sized cells with intensely hyperchromatic nuclei and varying amounts of clear or lightly eosinophilic cytoplasm In this field the stroma is abundant and consists of wavy bundles of connective tissue sprinkled with a moderate number of lymphocytes (Hematoxylin and eosin ×200)

pain, cough, and dyspnea. Examination of the chest was essentially normal, but roentgenograms revealed the presence of an anterior mediastinal tumor. In each case the patient was maintained on adequate doses of Neostigmine bromide, Diprostigmine, Mestinon, ephedrine sulfate and, at times, it was necessary to administer atropine to counter the effects of parasympathomimetic therapy. Elective tracheostomy 24 to 48 hours prior to thymectomy is extremely important in averting pulmonary complications; this was done in one patient. Had tracheostomy been performed in another, this patient would have survived pulmonary complications.

Thymectomy was performed through a median sternotomy. Following operation the patients improved and required less parasympathomimetic drugs.[10] Histologically, two of the tumors were benign and the third was a lymphosarcomatous type of malignant thymoma (Fig. 1, *A-C*). The malignant lesion was treated with radiation postoperatively and the patient is asymptomatic and greatly improved. One patient of this group with benign thymoma has been followed over 13 years and is doing well.

BENIGN THYMOMAS

Benign thymomas were found in patients whose ages ranged from 6 months to 26 years and the most common symptoms on admission were dyspnea, cough, chest pain, and wheezing. X-ray studies confirmed the presence of a mediastinal mass. Physical examinations were negative.

In one patient a thoracotomy was done; in a 6-month-old infant and in a 19-year-old woman with myasthenia gravis, median sternotomy was performed. Pathologic study confirmed the presence of thymic tumors. Generally patients were well and asymptomatic 10 years following operation.

MALIGNANT THYMOMAS

Of this type, the majority of lymphoepitheliomas and reticular cell varieties were found to be asymptomatic. The carcinomatous (Hassall's corpuscles, anaplastic) and Hodgkin's types were found to be symptomatic. In the patients without symptoms, routine x-ray studies usually disclosed the presence of a mass, whereas symptomatic patients complained of nonproductive cough, dyspnea, and chest pain. Physical examination of the chest disclosed evidence of a decrease in resonance and breath sounds with dullness to percussion.

Findings of tracheal narrowing, displacement of the tracheobronchial tree, or blood in the bronchus at bronchoscopy was of significant help in the diagnosis of malignant thymomas.

In one case, a reticular cell tumor surrounded all the vital vessels arising from the arch of the aorta. (Fig. 2, *E*). In another of the anaplastic carcinoma type, an incisional biopsy was performed followed by deep radiation therapy. In a third patient with Hodgkin's type of malignant thymoma, which filled the entire left hemothorax and was densely adherent to the lung radiation therapy was administered following excision of the tumor. Nine years following operation, chest roentgenograms showed no progression of the tumor.

NEUROGENIC TUMORS

Intrathoracic neurogenic tumors rank second to intrathoracic goiter as the most common mediastinal tumor (Fig 3, *A-E*). These tumors[14] arise from intercostal nerves or nerve sheaths, ganglion cells, sympathetic cells, and pheochromocytes. The majority are benign. Age and sex incidence in our series are given in Table III.

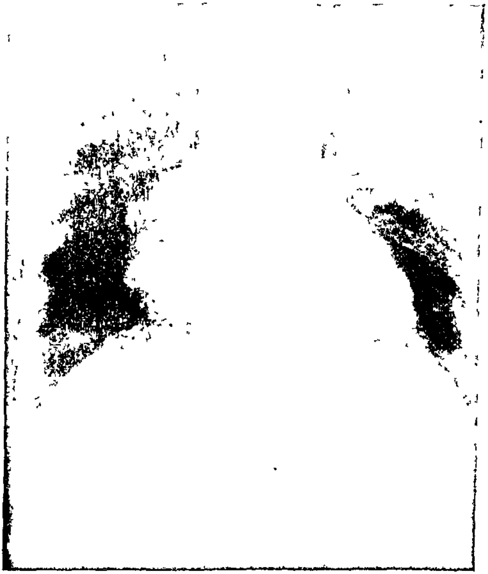


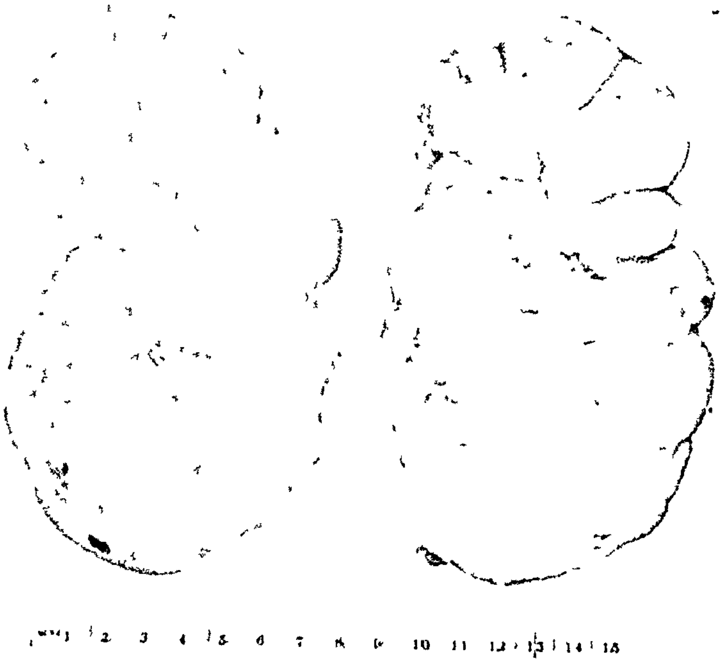
Fig 2 —Malignant thymoma. *A*, Lymphoepithelioma-chest x-ray film.

The *tumors are located predominantly in the paravertebral area of the* upper portions of the posterior mediastinum. Over 90 per cent were benign; neurofibroma being most common. Malignant sympathicoblastoma and neuroblastoma accounted for the malignant types.

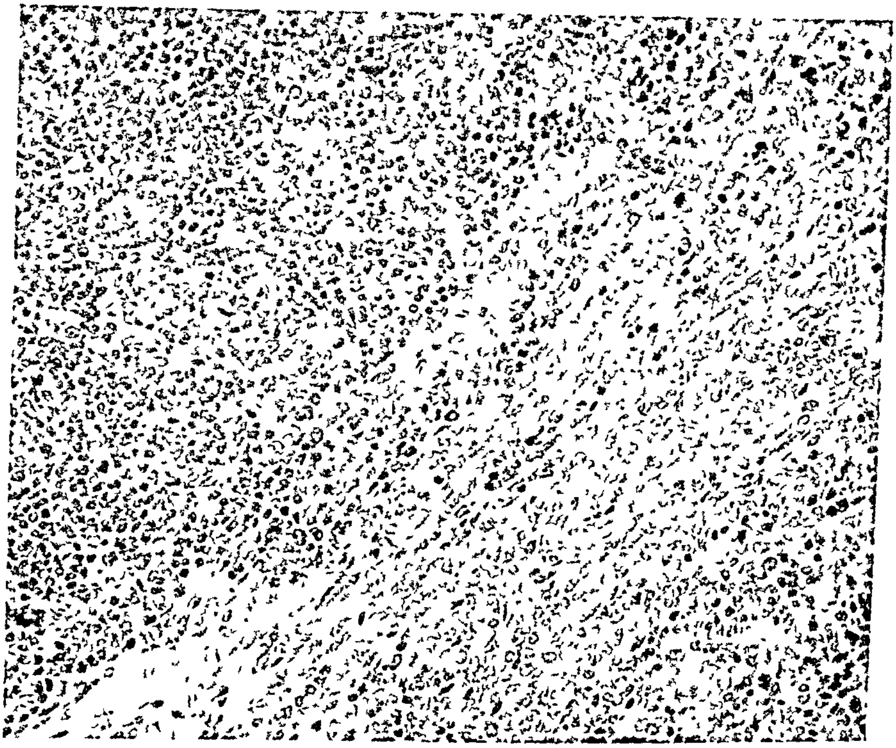
In one half of the patients, the chief complaint was dyspnea. Retrosternal pain was present in 3, 5 patients were asymptomatic. Roentgenograms were diagnostic in 6 of the cases. Histologic study of the surgical specimens confirmed the diagnosis in all cases.

A clinical history of chest pain, dyspnea, with roentgenographic evidence of a lobulated or round mass in the posterior or upper posterior mediastinum, is highly suggestive of a neurogenic tumor. As a rule, malignant neurogenic neoplasms cause pain

Surgery is the treatment of choice; radiation therapy has little effect upon this type of neoplasm Surgical intervention was attempted in 11 [illegible] and



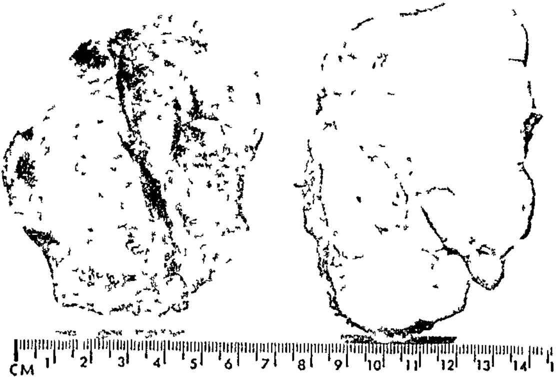
B.



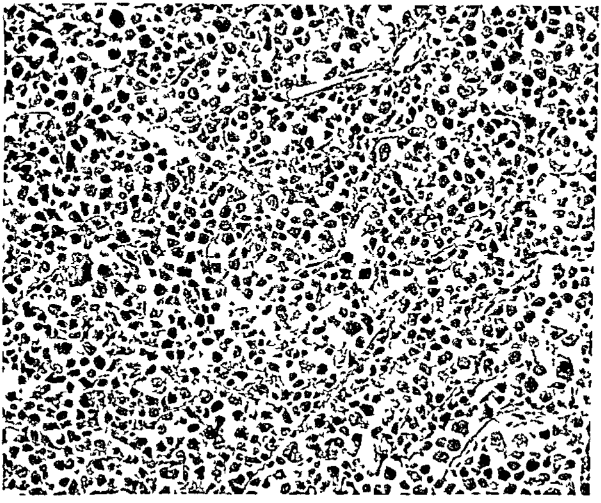
C.

Fig. 2—Cont'd *B,* Gross specimen of lymphoepithelioma

C, Microscopic section of so-called lymphoepithelioma of the thymus (thymoma) Side by side can be seen an area rich in small round cells with little or no discernible cytoplasm (lymphocytes) and one composed of elongated cells with oval, large, vesicular nuclei and scanty pale cytoplasm (Hematoxylin and eosin ×200.)



D



E

Fig 2—Cont'd D, Thymic carcinoma—Hassall corpuscle type Gross specimen
E Microscopic specimen of reticulum cell sarcoma involving the thymus The field is crowded by large cells with bizarre hyperchromatic nuclei and varying amounts of cytoplasm Delicate reticular fibers seen among the tumor cells can be demonstrated to a better advantage with appropriate special stains (Hematoxylin and eosin ×200)

excision of the tumor completed in 10. In over one half of the cases, at operation, the neoplasms were found fixed to the heads of the ribs, paravertebral area of the spinal column, or in the region of the first four ribs. In one case, the tumor extended from the neck to the ninth vertebra in the posterior mediastinum.

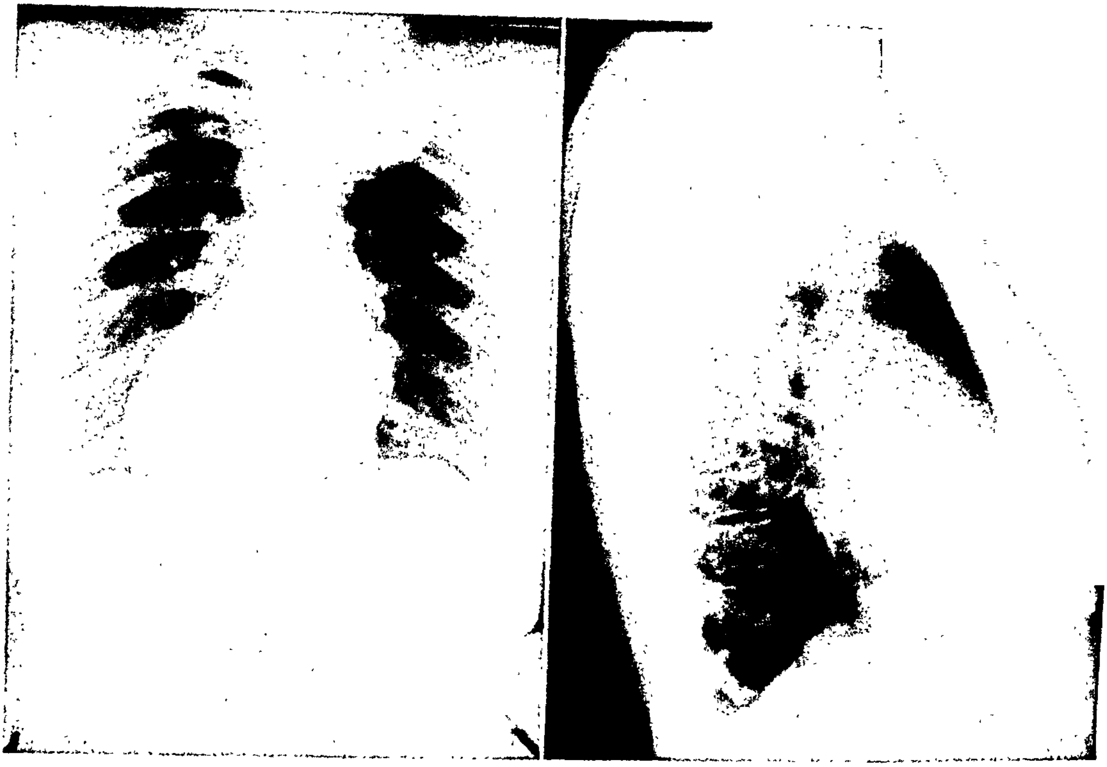

A. B.

Fig. 3.—Neurofibroma. *A*, Chest x-ray film—posteroanterior. *B*, Chest x-ray film—lateral.

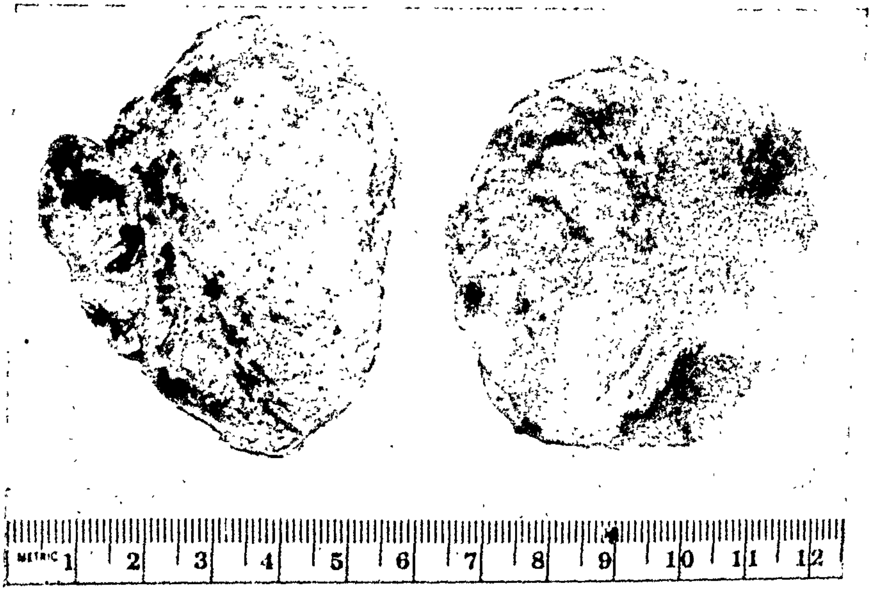


Fig. 3.—Cont'd. *C*, Gross specimen.

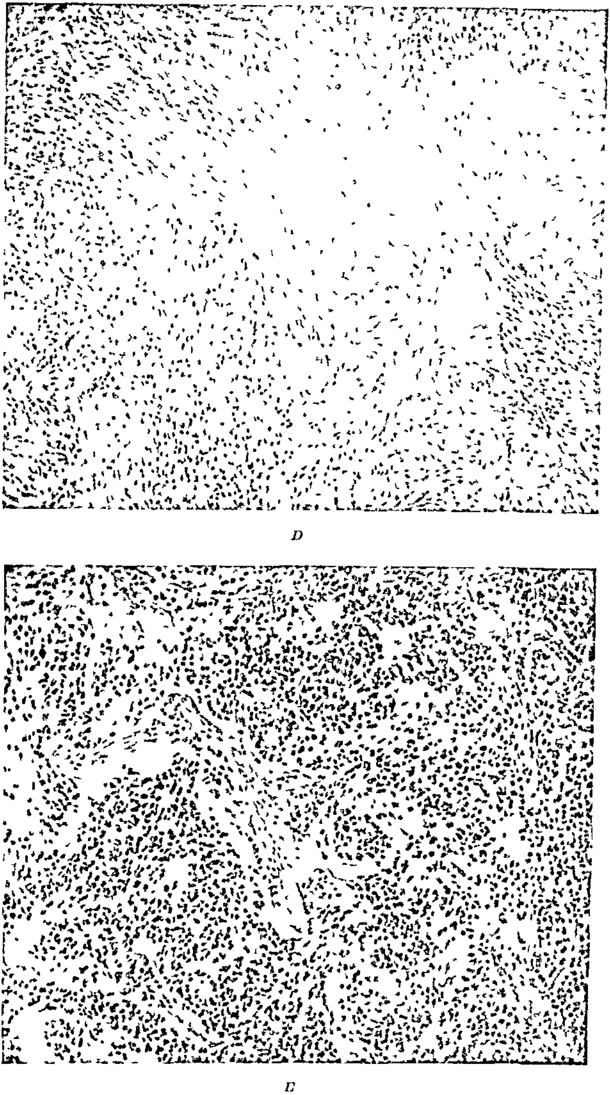


Fig 3—Cont'd *D*, Microscopic section of neurofibroma Compact bundles of spindle cells in palisade formation are seen Cystic degeneration and necrosis are absent. (Hematoxylin and eosin ×100)

E, Microscopic section of neuroblastoma. The tumor cells resemble mature lymphocytes, are small, round, or slightly oval, and possess little or no discernible cytoplasm Septa of connective tissue make up the scanty stroma (Hematoxylin and eosin ×200.)

TABLE III. NEUROGENIC TUMORS

Total Number of Cases	11
Age	
8 years to 58 years	
Average Age	
35.4	
Sex	
6 males—5 females	
Race	
10 white—1 Negro	
Diagnosis	
Benign neurogenic tumors	9
Malignant neurogenic tumors	2
Pathologic Types of Tumors	
Neurofibroma	8
Fibroneuroma and neuroblastoma	1
Neurolemmoma	1
Malignant sympathicoblastoma	1
Treatment	
Operative	
Thoracotomy and excision	10
Thoracotomy	1

Prognosis.—Of the 10 patients surviving operation, 8 are living after 5 years or more. The prognosis is good for neurofibroma or ganglioneuroma, if the tumor is completely removed.

TERATOID TUMORS AND CYSTS

Teratoid tumors and cysts may be classified according to their origin from the respective germ layers, i.e., epidermoid (ectodermal tissue), dermoid cysts (composition of ectodermal-mesodermal tissue), and teratomas (composition of ectodermal-mesodermal-entodermal tissue).

In seven different series totaling 396 cases,[1-7] 14.4 per cent were benign teratomas and 2.3 per cent were malignant. In the present report, this type of tumor ranked third, comprising 19.0 per cent of the total 42 cases reported (Table IV). The neoplasms were most frequently detected incidentally on chest roentgenograms, while others grew to such proportions as to compress adjacent structures, producing chest pain, dyspnea, hoarseness, weight loss, etc.

An opacity in the anterior part of the superior or middle mediastinum that contains bone, hair, or teeth, as visualized on roentgenograms, establishes the diagnosis. These tumors are potentially dangerous; they may rupture into the pleura, pericardium, aorta, or vena cava, thereby producing mediastinitis or infection; and some undergo malignant change and metastasize either by direct extension to adjacent structures, or distally by way of the lymphatics to the regional nodes or the liver. Therefore, when possible, complete excision is *mandatory.*

Of the dermoid cysts, two benign and one malignant type were operable and completely removed; one was diagnosed as malignant but was not operated upon, but autopsy revealed it to be malignant teratoma. Of two malignant teratomas, one was removed, but the patient died of recurrent

TABLE IV. TERATOMAS AND DERMOID CYSTS

Total Number of Cases	8	
Age		
19 years to 53 years		
Average Age		
36 years		
Sex		
6 females—2 males		
Race		
6 white—1 Negro		
Diagnosis		
Teratomas		
Benign		2
Malignant		2
Dermatoid cyst		
Benign		2
Malignant		2
Autopsy Diagnosis		
Nonoperative malignant dermoid cyst		1
Nonoperative malignant teratoma		1
Operative malignant teratoma		1
Treatment		
1. Operative		
Thoracotomy and excision		5
Thoracotomy and inoperable		1
2. Nonoperative		

malignant teratoma with extensive metastasis to the left lung, pericardium, and diaphragm, the other was inoperable. Both benign teratomas were completely excised.

MEDIASTINAL BRONCHOGENIC CYSTS

Cysts of the mediastinum are classified as pericardial, bronchogenic, thymic, and gastroenteric in origin (Table V).

TABLE V. INCIDENTAL TUMORS

Total Number of Cases	5	
Age		
45 years to 57 years		
Average Age		
50.5 years		
Sex		
3 females—2 males		
Race		
5 white		
Diagnosis		
Bronchial cyst		2
Hamartoma		1
Lipoma		1
Pericardial cyst		1
Treatment		
Thoracotomy and excision		4
Thoracotomy and left upper lobectomy		1

Ringertz and Lidholm,[4] Blades,[1] and others,[3, 5] found bronchogenic cysts to be the second most common mediastinal tumor. In Ringertz's series of 155 cases, bronchogenic cysts comprised 13.6 per cent of the total. In this paper bronchogenic cysts accounted for 4.8 per cent of the total of 42 primary mediastinal tumors. The origin has been ascribed to a small diverticulum adjacent to the respiratory anlage in the foregut. These may be located at any site in the mediastinum. Maier[17] classified bronchogenic cyst sites as paratracheal, carinal, hilar and paraesophageal, depending upon their attachment to the tracheobronchial system and to the esophagus. Although usually asymptomatic, they may produce signs and symptoms of tracheobronchial obstruction.

Diagnosis may be established by x-ray studies. Cysts are smooth and contain no calcium, osseous, or cartilaginous elements. They are located adjacent to the mediastinum and, at fluoroscopy, they may move on swallowing. In one patient with dyspnea and cough, an angiocardiogram was helpful and revealed a right superior mediastinal mass partially obstructing the superior vena cava. The cyst was completely excised and prognosis was excellent (Fig. 4).

Fig. 4.—Bronchial cyst. Gross specimen.

PERICARDIAL CYST

Pericardial coelomic cysts arise as a result of failure of fusion of the pericardial lacunae and are thin walled, lined by a layer of mesothelial cells, fibrous tissue and contain clear fluid. They are more commonly located in the anterior or middle mediastinum adjacent or adherent to the pericardium, pleura or diaphragm. The diagnosis may be suggested by the presence of a round opaque shadow in the cardiophrenic angle. A differential diagnosis between hernia of the foramen of Morgagni and lipoma must be considered.

Angiocardiogram was of aid in outlining a large pericardial cystic mass in a patient who was asymptomatic but whose chest roentgenogram demonstrated a mediastinal mass (Table V).

HAMARTOMA

Hamartoma is a rare benign tumor, composed of abnormally arranged tissue that may contain mesodermal and epithelial elements. The tumor is an incidental finding in asymptomatic patients usually in the sixth decade, undergoing x-ray studies. However, exertional dyspnea, substernal discomfort, or cough may exist. Diagnosis may be suspected if roentgenograms demonstrate a dense mass surrounded by normal pulmonary tissue and exhibiting sharp lobulated borders with areas of calcification.

Treatment is excision of the mass or a more radical operation such as lobectomy or pneumonectomy, depending upon the size of the tumor. The prognosis is generally excellent, but malignant transformation into an osteochondrosarcoma has been reported.

In the asymptomatic patient reported, a left upper lobectomy was performed for a round, well-delineated extradensity in the left upper lobe of the lung. Four years later, he was found in excellent health.

LIPOMA

Intrathoracic lipomas are rare tumors arising from connective tissue containing fat or fetal cells and are well encapsulated. As a rule they are confined to the thoracic cavity but may extend superiorly into the neck, inferiorly through the diaphragm, or anteriorly through the chest wall. The incidence of lipoma was found to be 2.3 per cent in a total of 396 cases representing the experience of seven groups[1-7] reporting mediastinal tumors. In our study, lipoma constituted 2.4 per cent of the total cases. Keely and Vana,[19] in a collective review of mediastinal lipomas, suggested the anatomic classification of intrathoracic and extrathoracic lipomas. The majority of mediastinal lipomas are primarily intrathoracic, usually asymptomatic, and may take on an hourglass appearance or attain such proportions as to induce mechanical pressure upon vital structures thus causing dyspnea, substernal oppression, cough, dysphagia, weakness, and other symptoms. An hourglass lipoma should be considered when a tumor in the neck or chest wall is continuous with the intrathoracic mass.

Treatment is surgical excision and this was done in the case reported. Follow-up 9 years after operation found this patient to be in excellent health.

SUMMARY

1. Seventy-four unselected mediastinal tumors were collected from the records, 1942-1956, of the Departments of Surgery and Oncology of the Jefferson Medical College and Hospital and 42 of these tumors were primary.

2. The characteristic clinical, pathologic, and roentgenologic features of the lesions are described. The variety of malignant thymomas and the association of myasthenia gravis with benign thymomas are emphasized.

3. Roentgenographic findings of a posterior mediastinal tumor is suggestive of a neurogenic neoplasm; the presence of cartilage, bone, teeth, etc., in a superior or middle mediastinal mass is compatible with a diagnosis of teratoid tumor. Lipoma should be considered when an hourglass type of opacity in the neck or chest wall is continuous with an intrathoracic mass. Roentgenograms demonstrating a dense mediastinal mass surrounded by normal pulmonary tissue and exhibiting a sharp lobulated and inner border of calcification is indicative of hamartoma.

4. Thoracotomy and excision of the mediastinal tumors were successfully performed in 36 of the cases. There was one supraclavicular node biopsy and 5 nonoperative cases.

The authors wish to express their appreciation and thanks to Dr. John H. Gibbon, Jr., and his associates for the use of their personal cases in this series.

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MYXOMA OF THE LUNG

James B. Littlefield, M.D., and E. Cato Drash, M.D., Charlottesville, Va.*

THE myxoma is a tumor whose histologic structure resembles primitive mesenchyme and contains a mucinous ground substance. Primary myxoma of the lung is rare and the resection of a solitary pulmonary mass diagnosed histologically as a myxoma prompted the review of this subject. Apparently the only other pulmonary neoplasm of this type previously reported was a "fibromyxoma" removed from the lung of an 8-year-old boy.[1]

CASE REPORT

A 54-year-old housewife was admitted to the Thoracic Surgical Service of the University of Virginia Hospital on Feb. 13, 1955. She complained of "a mass in my right lung" which was discovered on a routine 70 mm. roentgen film of the chest in November, 1954. A subsequent full-sized roentgenogram of the thorax taken in January, 1955, confirmed the presence of this lesion. It was not known how long the mass had been present. The patient had been in good health except for chronic "arthritis" of the lumbar and cervical spine and recurrent episodes of "sinusitis."

Physical examination revealed a well-nourished patient with moderate limitation of motion of the cervical spine and a quiescent, chronic, right, maxillary sinusitis. Roentgenograms and fluoroscopy of the chest showed a round, smooth, indeterminate mass, 2.5 cm. in diameter, without evidence of calcium at the level of the right third intercostal space (Fig. 1).

On Feb. 15, 1955, exploration of the right hemithorax revealed a 2 cm. globular, firm, well-circumscribed mass in the periphery of the posterior segment of the right upper lobe. A wedge resection of this lesion was performed, removing a liberal margin of normal pulmonary tissue. On section, the specimen was yellow-gray in color and frozen tissue examination demonstrated a benign neoplasm; the final pathologic diagnosis was a myxoma (Fig. 2).

The patient's postoperative course was uncomplicated and she has been entirely free of subjective symptoms related to her chest. Roentgenograms of the thorax 28 months after operation showed no evidence of tumor recurrence. The chronic "arthritic" symptoms have persisted.

Pathologic Description of the Tumor.—The tumor was a smooth, slightly lobulated mass buried in normal pulmonary tissue and measured 2.5 cm. by 1.5 cm. A thin capsule enclosed the lesion and there were no apparent pleural or bronchial communications. The cut surface was yellow-tan, firm and glistening, with softening in the central portion.

Microscopic sections showed the lesion to be sharply delineated from the surrounding compressed pulmonary tissue which formed a thin pseudocapsule. The tumor was composed of separate stellate cells with dense cytoplasm and coarse processes. The nuclei were ovoid

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From the Division of Thoracic Surgery, Department of Surgery, University of Virginia School of Medicine, Charlottesville, Va.

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*Research Fellow of the American Trudeau Society, Medical Section of the National Tuberculosis Association.

(10 to 30 microns in longest diameter) with fine regular chromatin and nucleoli that were indistinct even in the large cells. Between the cells and their processes were abundant amounts of a stringy, finely particulate, basophilic substance resembling mucin that stained positively with alcian blue and weakly with periodic acid-Schiff. No mitotic figures were apparent. A moderate number of thin-walled blood vessels were present and their walls were intimately bound with the tumor tissue. A light infiltration of lymphocytes, plasma cells, and polymorphonuclear leukocytes (eosinophilic and neutrophilic) were present throughout the tumor. These cells were concentrated about the larger blood vessels.

There was no evidence of vascular invasion by the tumor and no differentiated tissue elements such as cartilage, bone, fat or fibrous connective tissue were present.

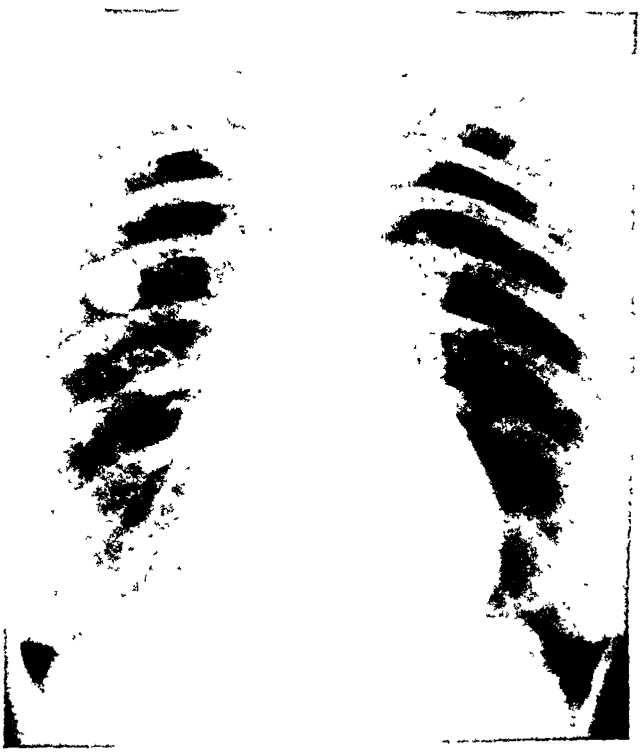

Fig. 1.—Preoperative roentgenogram showing the indeterminate lesion in the right upper lobe.

DISCUSSION

A great deal needs to be clarified about this group of tumors termed myxomas and accurate information is not easily obtained from the literature. Stout[2] in his classical paper has enumerated several reasons for this inaccuracy of classification.

1. Myxoid areas are sometimes present in a tumor composed predominantly of other tissue, such as the liposarcoma and rhabdomyosarcoma. Stout considers these tumors with "myxo" incorporated in their nomenclature (i.e., myxoliposarcoma) to have been erroneously classified as a variant of the true myxoma.

2. Myxosarcomas are classified in certain instances as belonging to the myxoma group; however, this seems inaccurate because myxosarcomas metastasize while myxomas, as defined by Stout,[2] do not metastasize.

3. The tendon sheath ganglions and skin lesions which resemble myxomas have sometimes also been included with the myxoma group.

4. There is considerable controversy regarding myxoid tumors of the heart. These are the *only neoplasms termed myxomas from which metastases have been* reported.[2, 3] This exception suggests that the metastatic tumors are probably sarcomas which appear as myxomas, or the apparent metastases might have been emboli and not true tumor dissemination.

These varied opinions make it difficult to classify and evaluate the behavior of the true myxoma.

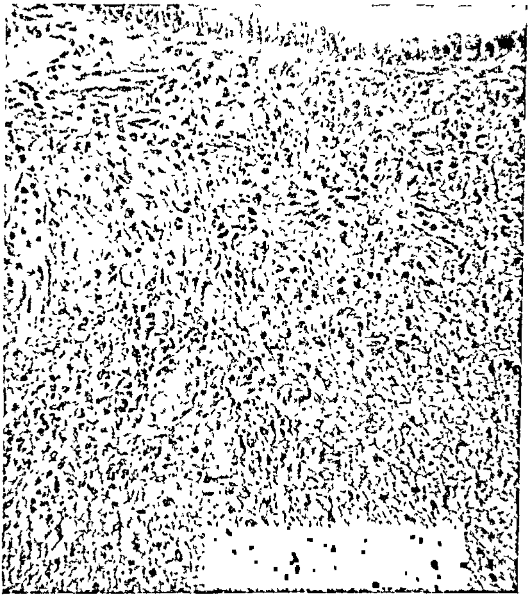

Fig 2.—Photomicrograph of the myxoma demonstrating the predominance of intercellular mucin and characteristic stellate cells (×250).

Incidence.—Stout,[2] in 1948, reviewed 143 myxomas exclusive of those of the heart. Seventy-two per cent of these lesions were either in the subcutaneous and aponeurotic tissue, bone, skin, or genitourinary tract—the incidence was approximately equal in the four sites. Eighteen per cent arose from the intestine, retroperitoneal tissue, sinuses, nares, joints, orbit, eyelids and muscle; 2 to 3 per cent were present in each location. Four per cent were from the pharynx and tonsil. The remaining 6 per cent arose from the spleen, appendix, liver, ear, parotid gland, or intracranial sites.

There were no pulmonary lesions in this series. Only one true myxoma has been previously reported from the lower respiratory tract. This lesion, removed from the lung of an 8-year-old boy, was described by Placitelli (1953) in the

Italian literature.[1] The tumor was the "size of a small egg" located in the apical-posterior segment of the left upper lobe. A wedge resection of the lesion was performed and 18 months after operation the patient was well without evidence of recurrence.

Clinical Characteristics.—The criteria for recognition of these tumors and their clinical and biologic behavior have been clarified by Stout.[2] No age or sex predominance is associated with the myxomas. The tumors grow slowly with intermittent periods of rapid enlargement and patients who were symptomatic with this lesion often waited as long as 4 years or more before seeking surgical treatment. There do not seem to be any outstanding clinical characteristics because many of the lesions are buried in bone or other deep structures. Perhaps the most consistent clinical characteristic of these tumors is their tendency to recur locally after inadequate excision.

Pathology.—The gross pathologic anatomy of myxomas is very similar to that of their fibroplastic counterparts except that the homogenous pale cut surface has a gelatinous, glistening appearance. Microscopically the basic cells are loosely arranged in a mucoid stroma or ground substance. This ground substance stains positively for mucoprotein or "mesenchymal mucus" and is probably largely hyaluronic acid. Fine reticulin fibers course through this stroma and between the cells. There may be moderate variations in the cell size and shape, anaplasia is slight and mitotic activity obscure. The cells may assume a fibroblastic appearance in the more dense areas. This appearance (fibroblastic) is the only degree of metaplasia that should be allowed in defining these tumors as true myxomas (Stout).

Many neoplasms composed primarily of cartilage, fat, fibrous or other tissue exhibit edematous areas which may or may not contain sufficient ground substance (mucoid stroma) to stain with mucin stains. The use of the prefix "myxo" in such instances (i.e., myxoliposarcoma) is confusing, because the behavior of these tumors is in accord with their dominant tissue and is not known to be modified by the presence of their "myxomatous" features. Such tumors do not meet the requirements of true myxomas.

The true myxoma then is a unicentric tumor which grows by infiltration and expansion of the initial lesion and histologically exhibits characteristic stellate cells with a predominance of intercellular mucin. Apparently it does not metastasize but threatens vital structures by its progressive growth.[4] The largest single group of tumors or tumor-like masses reported as myxomas have been found in the heart and it is questionable whether all of these tumors are true myxomas. Such tumors probably represent undifferentiated mesenchymal proliferation which may be either neoplastic, granulomatous, or thrombotic.

The use of the term "malignant myxoma" has been questioned. The only recorded instance of myxoma metastasis has been from a primary cardiac lesion.[3] Stout considers the myxoma malignant only because it often presents as an infiltrating growth which persistently recurs locally when not adequately excised and may eventually result in the patient's death This behavior differs from the usual benign tumor and seems to justify the use of the term malignant even though metastasis does not occur

Treatment —A biopsy of any suspected mesenchymal lesion should be performed whenever possible to establish the diagnosis so that a wide, primary excision may be planned and executed Inadequate initial operative removal results in recurrence of the tumor which is not usually fatal unless vital areas are invaded A patient, 65 years of age has been reported who had eight operations for a myxoma of the cervical region which repeatedly recurred over a 36 year period [5]

The exact extent of the infiltration that accompanies this tumor is often difficult to recognize grossly therefore, a wide initial excision of the lesion is the treatment of choice, except in bone where simple curettage has proved to be an effective procedure in several instances Radiation therapy has a limited usefulness in the treatment of myxomas

SUMMARY AND CONCLUSIONS

A primary myxoma of the lung has been reported which was successfully treated by resection without evidence of recurrence after 28 months One other similar lesion has been previously reported in the literature The pulmonary myxoma apparently exhibits the same histologic appearance and biologic behavior as myxomas which originate elsewhere in the body

Myxomas should be defined by strict histologic criteria including their characteristic stellate cells and prominent intercellular mucinous stroma Accepting these criteria, tumors composed primarily of other tissue elements are excluded The myxoma is basically a benign tumor with a tendency to repeated local recurrence

The biopsy of a suspected mesenchymal tumor should be performed whenever possible before treatment is begun Experience with extrapulmonary myxomas demonstrates that successful treatment depends upon a wide, initial surgical excision Radiation therapy is of limited usefulness

We wish to express our appreciation to Dr David E Smith, Chairman, Department of Pathology, for his assistance in the preparation of this manuscript

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BRONCHIOLAR (PERIPHERAL LUNG) NEOPLASMS AND PREVIOUSLY UNDESCRIBED OBSERVATIONS ON THE ORIGIN OF BRONCHIOLAR CARCINOMA

Stanton L. Eversole, Jr., M.D., and William F. Rienhoff III, M.D.,
Baltimore, Md.

INTRODUCTION

IN ROUTINE autopsy material, one very occasionally finds a subpleural nodule which on histologic examination is found to be a small bronchiolar adenomatous tumor or malformation (see Figs. 1, 2, 3, and 4). These lesions usually are only a few millimeters in diameter, but may be larger. Their subpleural location and, in the very small ones, their obvious relationship to bronchioles is very characteristic. While these little tumors are not common they certainly are not rare. In our material no examples of multiple tumors were found, although no special search for them was made and, because of their size, they could easily have been overlooked. We have regarded these lesions as inconsequential incidental findings until recent years when, in the surgical pathology laboratory, two similar localized tumors, but much larger and showing some histologic evidence of malignancy, have been encountered. Both of these lesions were asymptomatic, having been detected as incidental findings in routine chest x-ray studies. These clinically evident cases prompted us to peruse the literature and to our astonishment no references to benign tumors of this type were readily found. In the numerous reports on bronchiolar carcinoma and pulmonary adenomatosis only one mention of such a localized and innocuous lesion (as is depicted in Figs. 1 and 2) is described. Laipply, Sherrick, and Cape,[1] in presenting cases of bronchiolar tumors (by which term they mean bronchiolar carcinoma, pulmonary adenomatosis, etc.) pictured one small tumor and characterized it as the "smallest bronchiolar adenoma yet described." We were also surprised that these little tumors have not been given attention as possible foci of origin for bronchiolar carcinoma because certainly, in the larger lesions, there are many histologic features common to both.

Cases 1, 2, 3, and 4 are presented as definitely benign adenomatous malformations of the bronchioles. Cases 6 and 7 are examples of bronchiolar

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From the Departments of Pathology and Surgery, the Johns Hopkins University School of Medicine and Hospital, Baltimore, Md.

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carcinoma which bear a striking resemblance to the benign adenomatous malformations and we propose that the tumors arose from similar malformations. Case 5, an example of localized pulmonary adenomatosis is presented *only to contrast the histology of this disease with that of bronchiolar carcinoma.*

CASE REPORTS

Case 1.—(A. N. 20637.) This 58 year old Negro woman died of carcinoma of the pancreas which involved the ampulla of Vater producing obstructive jaundice. In addition to the primary pancreatic carcinoma there were mesenteric lymph node metastases, acute cholangitis, and liver abscesses.

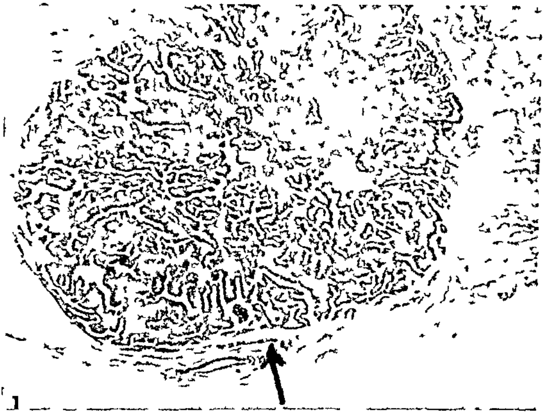

Fig. 1.—Case 1. The small tumor is shown in its entirety. The arrow points to a bronchiole associated with the tumor nodule. This little tumor is circumscribed but not encapsulated. The thick fibrous septa are continuous with the alveolar septa. One portion of the tumor is composed of solid masses of hyaline. The epithelium forms a single layer of cells on the thick fibrous septa. No mucus is formed by these cells. (Autopsy No. 20637.)

In the left lung (lobe not stated) was a 3 mm. well circumscribed but not encapsulated subpleural nodule (Fig. 1) which extended out of a bronchiole. The tumor was composed of thick fibrous septa with columnar, nonciliated, and nonmucus forming epithelium. The fibrous septa blended in with the alveolar septa at the margins of the tumor. The epithelial cells had scanty cytoplasm. The center of the tumor was hyalinized. The other sections of the lung were normal. This little tumor is obviously a benign adenoma.

Case 2.—(A. N. 25289.) This 64 year old Negro man died of massive intestinal hemorrhage. Emergency laparotomy revealed numerous colonic adenomatous polyps and, histologically, one of these showed extensive fresh hemorrhage. Postoperatively, the patient remained in shock and died. Other than extensive arteriosclerosis and hypertrophy of the left ventricle, the autopsy revealed only a number of benign adenomatous polyps in the transverse colon.

Microscopically, one section of lung showed an irregular but circumscribed nodule separated from the pleura by a very narrow rim of lung parenchyma (Fig. 2). The lobe from which this came was not known. The nodule was composed of thick fibrous septa which were lined by cuboidal and columnar nonciliated and nonmucus-forming epithelium. At one margin, the little tumor was continuous with a bronchiole; otherwise, the lung was normal. This tiny nodule is obviously an adenomatous malformation.

CASE 3.—(A. N. 12071) This patient was a 70-year-old white man who died of lymphosarcoma. The autopsy showed huge masses of retroperitoneal lymph nodes, and tumor replacing the left adrenal, infiltrating the diaphragm and tail of the pancreas. Histologically, the tumor was composed of small lymphocytes.

The pulmonary lesion was a 1.5 cm. nodule in the left upper lobe beneath the pleura which was umbilicated by the underlying tumor (Fig. 3). Histologically, this showed thick fibrous trabeculae which arborized and fused in a complicated manner. Lining the trabeculae was a single layer of epithelium which in places was thrown up into papillomatous folds. However, the epithelium was not overabundant and the rounded epithelial cells were not packed closely together, producing a cobblestone-like surface to the clefts. The epithelial cells had scanty cytoplasm and large nuclei. No cilia and no mitoses were seen. The thick fibrous trabeculae, in appropriate stains, showed masses of elastic fibers. The base of the tumor at the pleura was composed of hyaline tissue in which were numerous large blood vessels, but only occasional remnants of epithelium. The tumor was circumscribed but not encapsulated. The fibrous trabeculae were continous with the alveolar septa and the clefts merged with the alveoli. This small nodule is a benign adenomatous tumor or malformation.

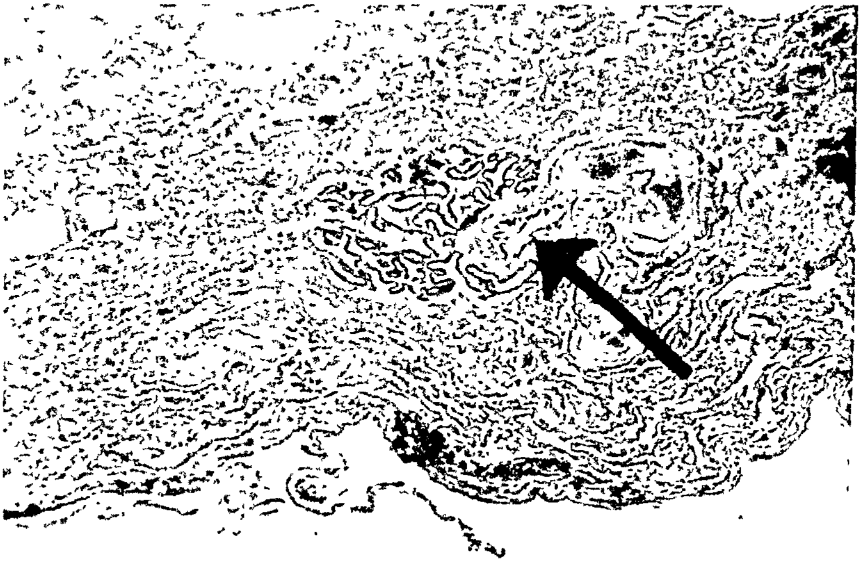

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Fig. 2.—Case 2. This minute subpleural nodule shows its circumscription and lack of capsule. The thick hyaline septa are covered by a single layer of cuboidal epithelium. The arrow points to a bronchiole associated with the tumor (Autopsy No. 25289).

CASE 4.—(A. N. 16648) This 76-year-old white diabetic woman died of generalized peritonitis following resection of an adenocarcinoma of the transverse colon because of leakage at the suture line. No metastases were found.

In the right upper lobe was a 1 cm. subpleural nodule which was sharply outlined (Fig. 4). Microscopically, the nodule was composed of thick fibrous septa which were lined by nonciliated cuboidal epithelium which had scanty cytoplasm. The cells produced no mucus, were not ciliated, and their large nuclei showed no mitoses. Adjacent to the pleura, the tumor was hyalinized and several rather large arteries were present in this area. No relationship to a bronchiole was seen in the sections available for study. Histologically, this nodule is obviously a benign adenomatous malformation or tumor.

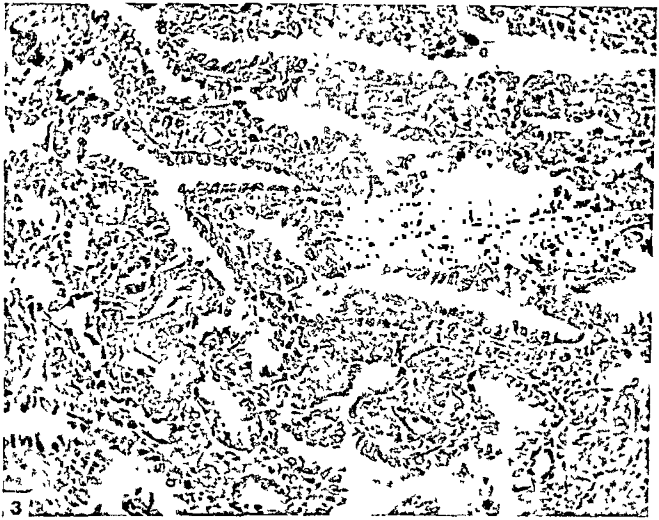


Fig 3 —Case 3 The thick fibrous septa are covered by a single layer of cuboidal nonmucus-forming epithelium The nuclei fill most of the rather shrunken epithelial cells These cells are not closely packed together producing an irregular surface to the clefts (Autopsy No 12071)

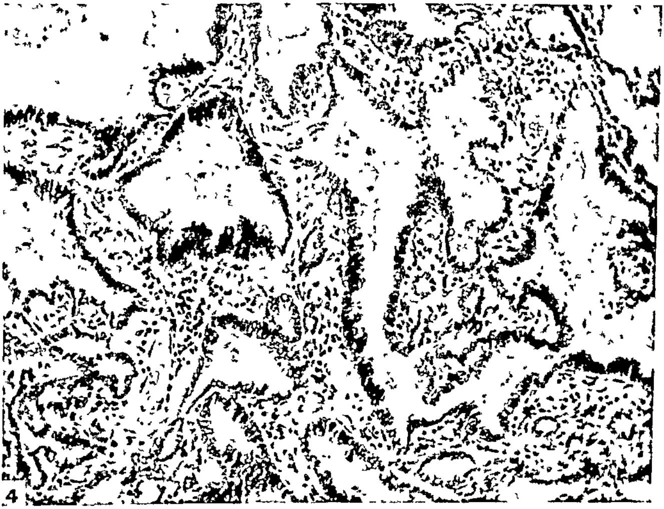


Fig 4 —Case 4 The thick fibrous septa are covered by cuboidal nonmucus-forming epithelium The epithelial cells vary in height giving an irregular appearance to the clefts (Autopsy No. 16648).

CASE 5.—(A. N. 15612) This 68-year-old white woman died of congestive heart failure. The autopsy revealed generalized arteriosclerosis with arteriosclerotic narrowing of the coronary arteries. The left ventricle was dilated and hypertrophied and there was extensive myocardial scarring.

In the left upper lobe there was a 1 cm. tumor nodule just beneath the pleura (Fig. 5). Histologically, this showed tall columnar cells lining delicate alveolar septa. The cells were not ciliated and their nuclei lay uniformly at the basal ends of the cells. These cells were uniformly distended with mucus and there was mucus in the alveolar spaces. The pleura was impinged upon, but not invaded and the lesion was sharply circumscribed. There were several bronchioles incorporated into the tumor, but these were intact. This is an example of a single small nodule of pulmonary adenomatosis.

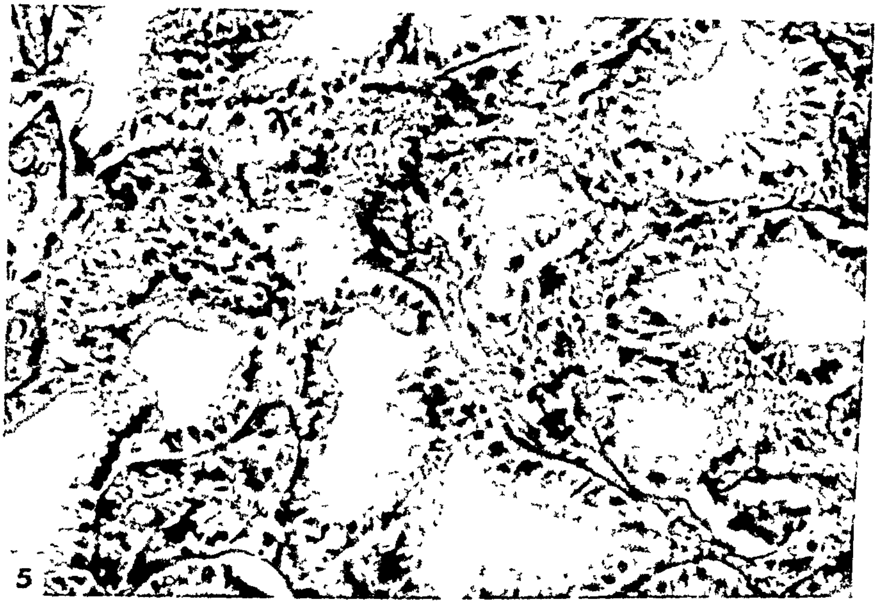


Fig. 5.—Case 5. The tall columnar mucus-producing epithelium forms a one cell layer membrane lining of alveolar septa. The nuclei lie at the base of the cells. The alveolar septa are not thickened or appreciably scarred (Autopsy No. 15612).

CASE 6.—(H. N. 795575) This 69-year-old white man was admitted to the Johns Hopkins Hospital for evaluation of a shadow, demonstrated by x-ray, in the upper portion of the right lung. His family and past history were not pertinent. Except for the year prior to this hospitalization, the patient had had x-ray studies of the chest annually for 12 years as part of routine physical examinations. The roentgenogram taken a few weeks prior to this hospitalization revealed a density in the right upper lobe (Fig. 6). He was entirely free of respiratory symptoms and his general health was excellent. The physical examination and laboratory studies revealed no abnormalities. The old roentgenograms were obtained for review and they were all normal except for the last one, taken 2 years previously. In retrospect, this showed a probable small density appearing in the right first interspace anteriorly. Tomograms were made and these revealed no calcification in the lesion. Other x-ray studies to rule out a possible primary tumor elsewhere were negative. The old tuberculin skin test was positive (1:1000). A right scalene lymph node biopsy showed no abnormalities. Through a right anterolateral incision, a thoracic exploration was performed. Beneath a puckering of the pleura, a small mass was noted near the apex of the right upper lobe. This was biopsied and a frozen section revealed it to be a tumor, thought to be primary in the lung. The right middle lobe was partially atelectatic and near its hilum a firm rounded calcified mass was seen. The lower lobe and the mediastinum seemed normal.

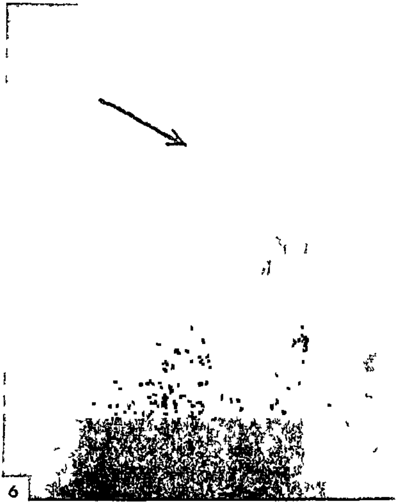


Fig. 6.—Case 6. Laminogram of chest showing ill defined density in right upper lung area (upper portion of density marked by arrow).

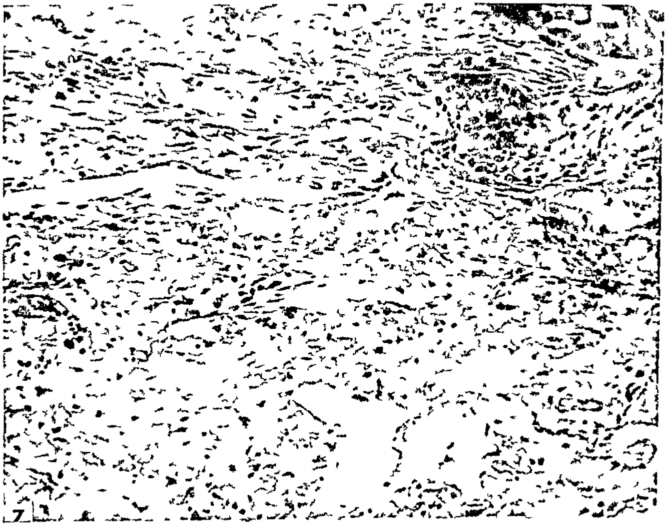


Fig. 7.—Case 6. The hyaline core of the tumor is almost devoid of epithelium. Numerous endothelial lined channels are seen. In such areas there are dense masses of elastic fibers.

Right upper and middle lobectomies were performed. The patient withstood the operative procedure well, the postoperative course was uneventful, and he was discharged on the fifteenth postoperative day. Ten months later his local physician reported him to be well, but no further x-ray studies had been made.

The gross specimen (S. P. No. 58-244) of the lung (right upper and middle lobe) showed two lesions; one beneath a dimpling of the pleura in the apical segment of the upper lobe and the other a firm 2 cm. nodule on the medial and inferior surface of the middle lobe near the right middle lobe bronchus. On cutting the apical lesion, there was an ill-defined 3 cm. nodule in the lung parenchyma with its base abutting on the pleura. This base of the tumor was cheesy in consistency and white. The borders of the tumor were ill defined. No bronchial communication was found. The middle lobe lesion was well circumscribed and did not connect with the middle lobe bronchus. On section, it was yellow with flecks of black anthracotic pigment in it. Careful opening of the major bronchi revealed no lesions.

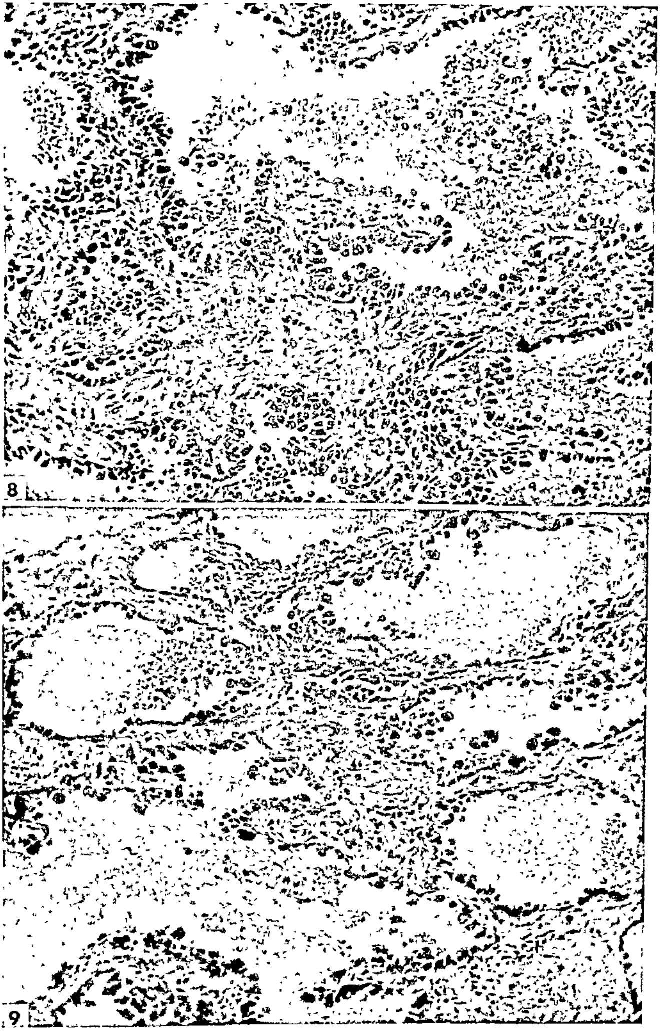
The histologic sections of the tumor nodule from the apical segment of the upper lobe showed extensive hyalinization in the base of the tumor abutting onto the pleura (Fig. 7). In this hyaline area, there were some epithelial cells forming acini or cysts with papillary projections. Elsewhere there were thick fibrous trabeculae which at the junction with the normal lung were seen to be continuous with the alveolar septa. These thick trabeculae were lined by cuboidal epithelial cells. Their free margins were rounded and as the cells did not lie very close together on the septa they produced an irregular cobblestone effect (Figs. 8 and 9). In places, the epithelium formed delicate papillary projections into the cystic spaces. Nowhere was mucus produced by the cells, but many epithelial cells lay free in the cystic spaces. The tumor cells had rather large nuclei and little cytoplasm. No mitoses were seen. In the hyalinized core were residual nests of tumor cells which in places formed cystic spaces, but in places the cells were more compact and had an epidermoid appearance (Fig. 10). The epithelium in the hyalinized areas grew in a more irregular manner than elsewhere. Several large cystic bronchioles were present in the hyalinized areas and they had ciliated columnar epithelium.

In appropriate stains, the thickened trabeculae showed much more elastic tissue than was present in the normal alveolar septa (Fig. 11). In the hyalinized portions, there was also a great amount of elastic tissue, but there the possibility of collapse and concentration of the elastica could not be ruled out. However, the elastic tissue in the thickened alveolar septa was continuous with the normal elastica in the alveolar septa.

The nodule from the hilum of the middle lobe showed typical lipoid pneumonia (Fig. 12). Numerous giant cells, containing single large lipoid vacuoles as large as alveoli, were present and interstitial deposition of lipoid was seen. Extensive hyaline scar and chronic inflammation were present. Several small bronchi were involved in the lipoid pneumonia and, in one such bronchus, there was a microscopic tumor-like nodule growing down into the adjacent tissue (Fig. 13). The bronchial epithelium was ulcerated at this site. The cells of this small tumor grew in solid sheets and were entirely different from those of the apical lesion. This lesion probably is similar to the solid epithelial growths which are seen in cases of congenital cystic lungs.[9] In our opinion, this lesion was not related in any way to the apical tumor. The peribronchial lymph nodes were free of tumor as was the rest of the lung.

The upper lobe lesion was diagnosed as a low-grade bronchiolar carcinoma. The middle lobe lesion was diagnosed as focal lipoid pneumonia with a focus of peculiar epithelial proliferation and downgrowth from a small bronchus.

CASE 7.—(H. N. 708531) This patient was a 53-year-old male chemist who was admitted for evaluation of a pulmonary density noted on a routine chest roentgenogram. The family and past history were negative. The patient had undergone annual physical examinations including x-ray studies of the chest for the previous 15 years. Five years



Figs. 8 and 9.—Case 6. The thick fibrous septa are covered by rounded cuboidal cells which secrete no mucus. The epithelial cells are not closely packed together on the septa and this produces the irregular surface of the clefts. (Surg. Path. 58-241.)

Right upper and middle lobectomies were performed. The patient withstood the operative procedure well, the postoperative course was uneventful, and he was discharged on the fifteenth postoperative day. Ten months later his local physician reported him to be well, but no further x-ray studies had been made.

The gross specimen (S. P. No. 58-244) of the lung (right upper and middle lobe) showed two lesions; one beneath a dimpling of the pleura in the apical segment of the upper lobe and the other a firm 2 cm. nodule on the medial and inferior surface of the middle lobe near the right middle lobe bronchus. On cutting the apical lesion, there was an ill-defined 3 cm. nodule in the lung parenchyma with its base abutting on the pleura. This base of the tumor was cheesy in consistency and white. The borders of the tumor were ill defined. No bronchial communication was found. The middle lobe lesion was well circumscribed and did not connect with the middle lobe bronchus. On section, it was yellow with flecks of black anthracotic pigment in it. Careful opening of the major bronchi revealed no lesions.

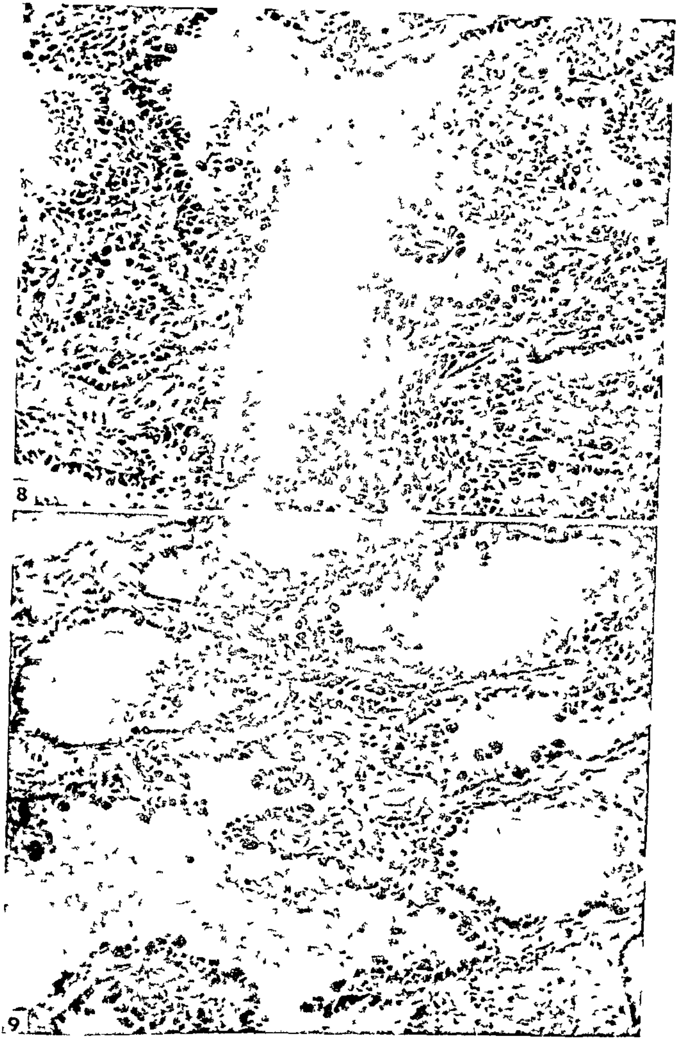
The histologic sections of the tumor nodule from the apical segment of the upper lobe showed extensive hyalinization in the base of the tumor abutting onto the pleura (Fig. 7). In this hyaline area, there were some epithelial cells forming acini or cysts with papillary projections. Elsewhere there were thick fibrous trabeculae which at the junction with the normal lung were seen to be continuous with the alveolar septa. These thick trabeculae were lined by cuboidal epithelial cells. Their free margins were rounded and as the cells did not lie very close together on the septa they produced an irregular cobblestone effect (Figs. 8 and 9). In places, the epithelium formed delicate papillary projections into the cystic spaces. Nowhere was mucus produced by the cells, but many epithelial cells lay free in the cystic spaces. The tumor cells had rather large nuclei and little cytoplasm. No mitoses were seen. In the hyalinized core were residual nests of tumor cells which in places formed cystic spaces, but in places the cells were more compact and had an epidermoid appearance (Fig. 10). The epithelium in the hyalinized areas grew in a more irregular manner than elsewhere. Several large cystic bronchioles were present in the hyalinized areas and they had ciliated columnar epithelium.

In appropriate stains, the thickened trabeculae showed much more elastic tissue than was present in the normal alveolar septa (Fig. 11). In the hyalinized portions, there was also a great amount of elastic tissue, but there the possibility of collapse and concentration of the elastica could not be ruled out. However, the elastic tissue in the thickened alveolar septa was continuous with the normal elastica in the alveolar septa.

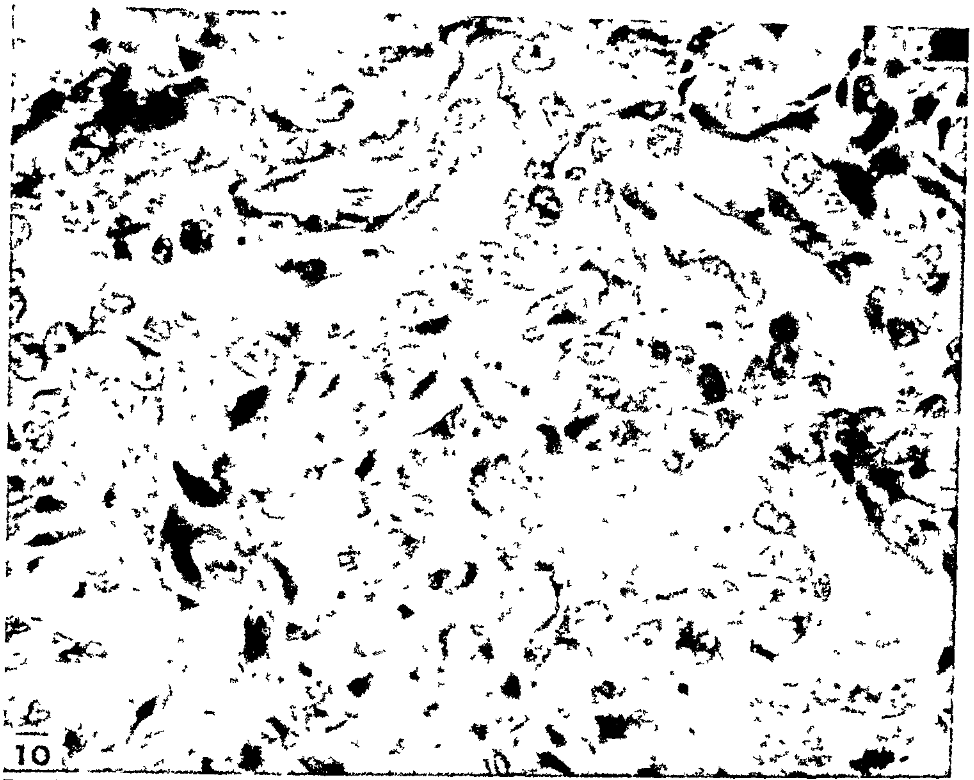
The nodule from the hilum of the middle lobe showed typical lipoid pneumonia (Fig. 12). Numerous giant cells, containing single large lipoid vacuoles as large as alveoli, were present and interstitial deposition of lipoid was seen. Extensive hyaline scar and chronic inflammation were present. Several small bronchi were involved in the lipoid pneumonia and, in one such bronchus, there was a microscopic tumor-like nodule growing down into the adjacent tissue (Fig. 13). The bronchial epithelium was ulcerated at this site. The cells of this small tumor grew in solid sheets and were entirely different from those of the apical lesion. This lesion probably is similar to the solid epithelial growths which are seen in cases of congenital cystic lungs.[9] In our opinion, this lesion was not related in any way to the apical tumor. The peribronchial lymph nodes were free of tumor as was the rest of the lung.

The upper lobe lesion was diagnosed as a low-grade bronchiolar carcinoma. The middle lobe lesion was diagnosed as focal lipoid pneumonia with a focus of peculiar epithelial proliferation and downgrowth from a small bronchus.

CASE 7.—(H. N. 708531) This patient was a 53-year-old male chemist who was admitted for evaluation of a pulmonary density noted on a routine chest roentgenogram. The family and past history were negative. The patient had undergone annual physical examinations including x-ray studies of the chest for the previous 15 years. Five years



Figs 8 and 9 —Case 6 The thick fibrous septa are covered by rounded cuboidal cells which secrete no mucus The epithelial cells are not closely packed together on the septa and this produces the irregular surface of the clefts (Surg Path 58 214)



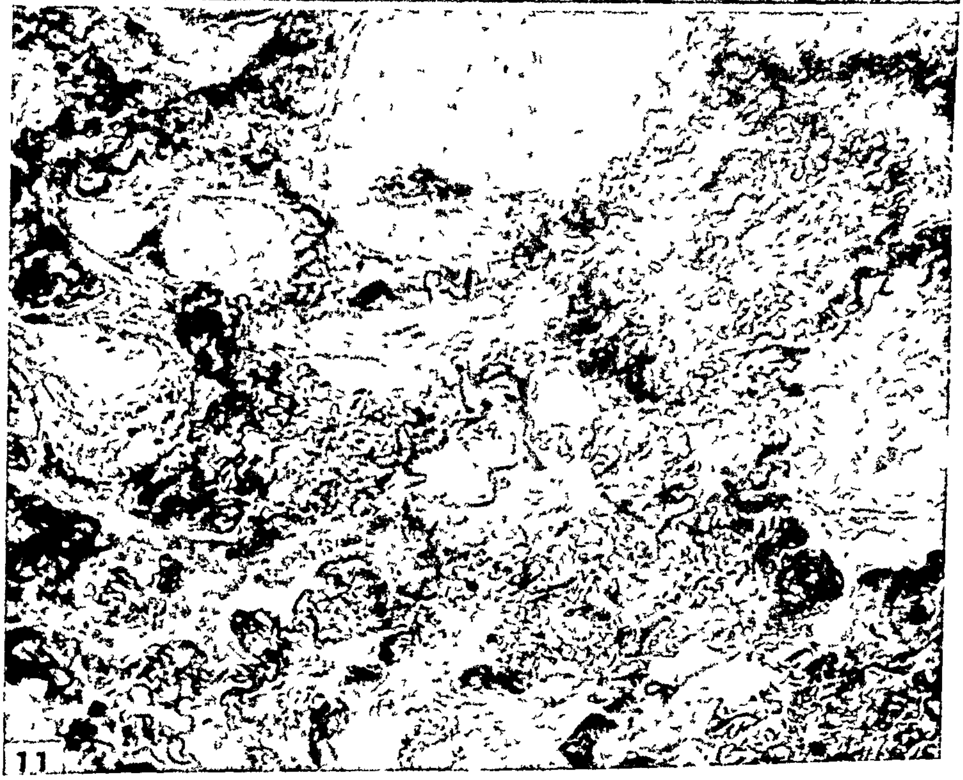
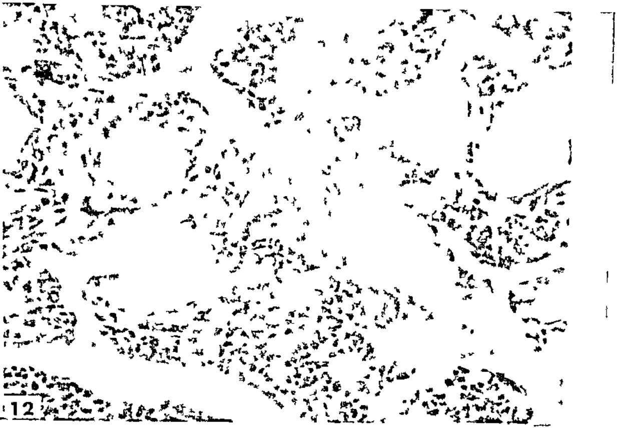


Fig 10 —Case 6. In the hyaline core are foci of large irregular epithelial cells Such areas are thought to represent some degree of malignancy

Fig 11.—Case 6. A great deal of elastic tissue is present in the fibrous septa The epithelial cells stain faintly in this section (Verhoeff-van Gieson's stain). In the hyalinized areas are dense masses of elastic fibers.



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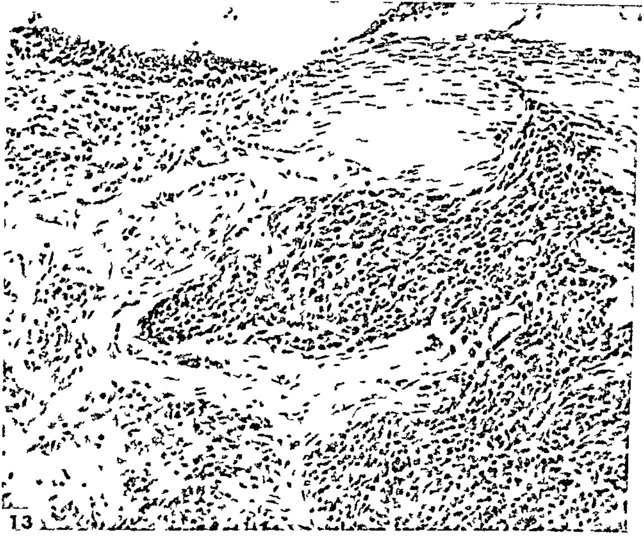

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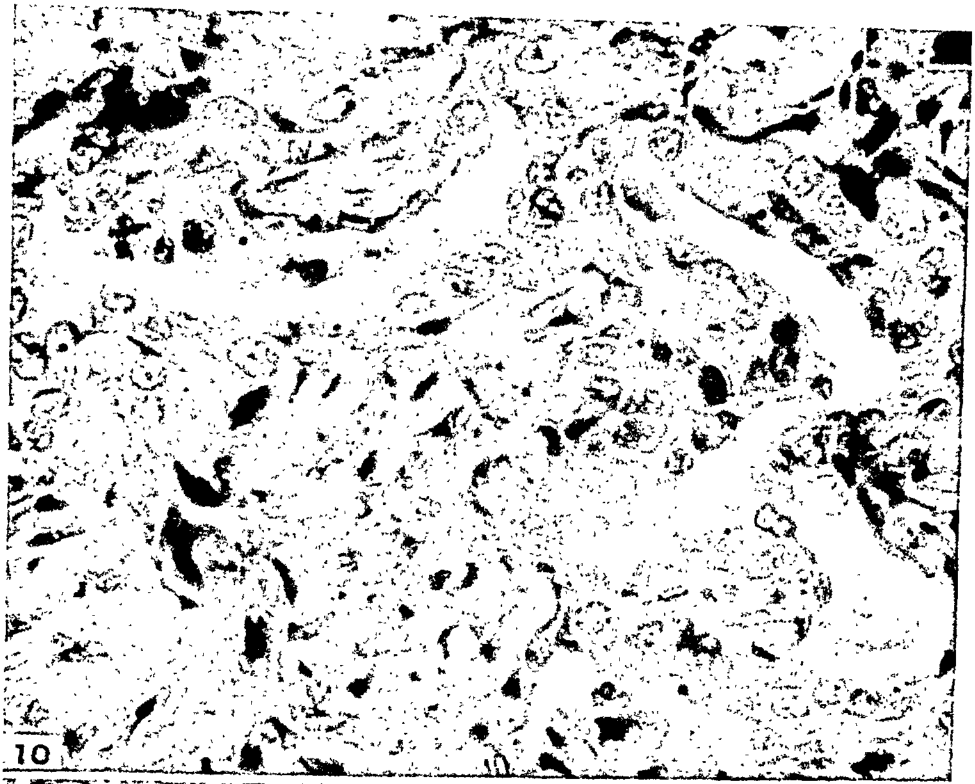
Fig 12 —Case 6 The nodules from the hilar region of the right middle lobe show typical lipoid pneumonia. The rounded clear spaces are vacuoles which contained lipoid The vacuoles are in macrophages giant cells and free in the alveolar septa Numerous lymphocytes are present

Fig 13 —Case 6 In the nodule of lipoid pneumonia a small bronchus (top of figure) shows an ulceration with underlying scarring Beneath this is a solid mass of abnormal epithelium This epithelial proliferation is entirely different from the upper lobe lesion



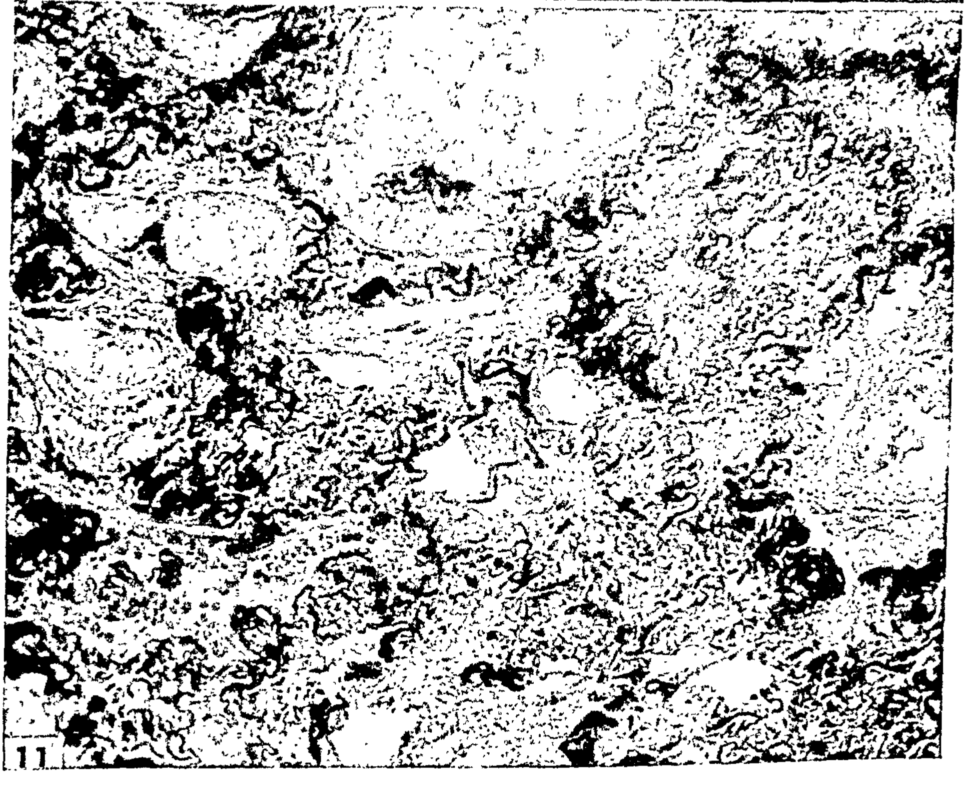
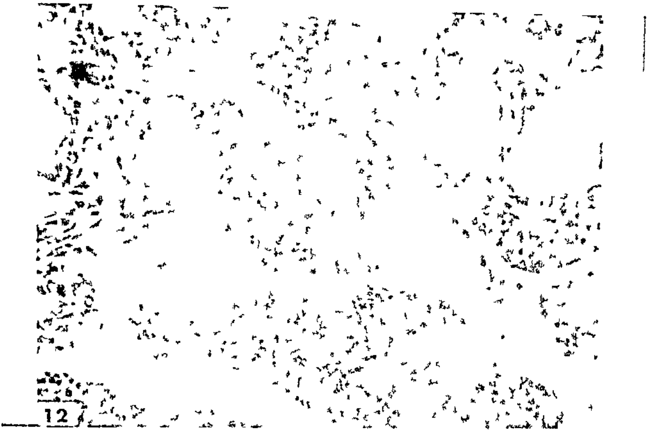


Fig. 10.—Case 6. In the hyaline core are foci of large irregular epithelial cells. Such areas are thought to represent some degree of malignancy.

Fig. 11.—Case 6. A great deal of elastic tissue is present in the fibrous septa. The epithelial cells stain faintly in this section (Verhoeff-van Gieson's stain). In the hyalinized areas are dense masses of elastic fibers.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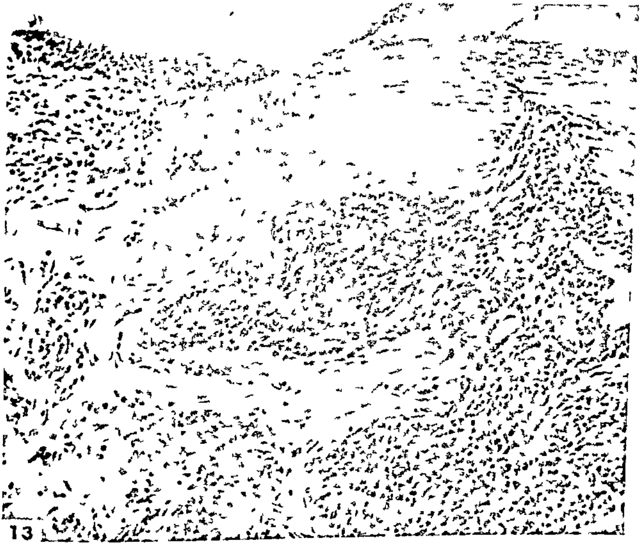
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Fig 12—Case 6 The nodules from the hilar region of the right middle lobe show typical lipoid pneumonia The rounded clear spaces are vacuoles which contained lipoid The vacuoles are in macrophages, giant cells and free in the alveolar septa Numerous lymphocytes are present

Fig 13—Case 6 In the nodule of lipoid pneumonia a small bronchus (top of figure) shows an ulceration with underlying scarring Beneath this is a solid mass of abnormal epithelium This epithelial proliferation is entirely different from the upper lobe lesion

previously, a small density was noted in the right upper lobe area. In the ensuing years, the lesion was noted to increase in size somewhat, particularly in the 18 months prior to this admission. He had no symptoms of any sort. The admission physical examination and laboratory studies were within normal limits. The old tuberculin skin test was positive in the 1:10,000 dilution. The roentgenogram revealed a small lesion in the right upper lobe area (Fig. 14). Tomograms revealed two calcific densities associated with, but not actually in, the lesion. Cultures for acid-fast bacilli were negative. Exploration was decided upon and, on the fifth hospital day, a right upper lobectomy was performed. At operation, the mass was located posteriorly in the right upper lobe and measured about 5 cm. in diameter. There was no evidence of involvment of the mediastinal lymph nodes or of the right middle or lower lobes. The postoperative course was uneventful and the patient was discharged on the fourteenth postoperative day.

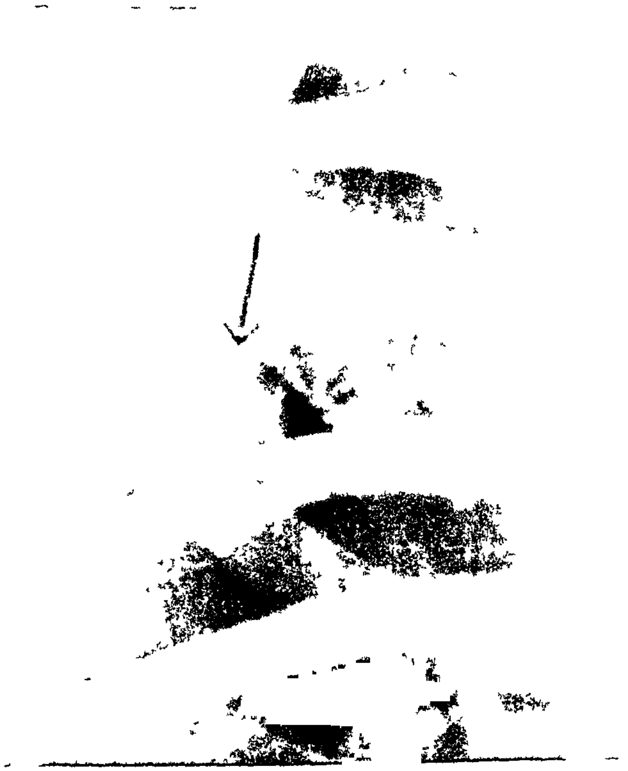

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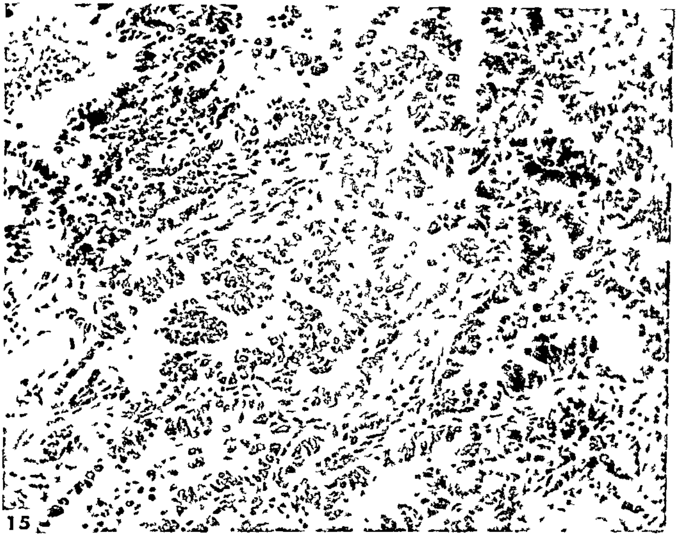
Fig. 14.—Case 7. Radiogram of chest showing ill-defined infiltration in right upper lung area (see arrow).

He was seen 30 months after the operation and at that time was doing well. His chest roentgenogram showed no lesion.

The gross specimen (S. P. No. 55-3154) consisted of the right upper lobe of the lung and there was a small puckering of the pleura over the apical posterior segment. On section, dense cheesy material of a gritty consistency underlay the dimpled pleura. The tumor fanned out from this and blended in with the lung so that grossly its margins were hard to define. It was not encapsulated. The tumor had no bronchial relationship and the major bronchi were normal.

The microscopic sections showed the tumor to be composed of rather thick trabeculae which were lined by columnar or cuboidal cells (Fig. 15). The free margins of the cells were rounded and the cells were uneven in height. As they were not very closely packed onto the trabeculae the epithelial surface had a cobblestone appearance. There was no capsule and the trabeculae blended in with the alveolar septa (Fig. 16). The nuclei were



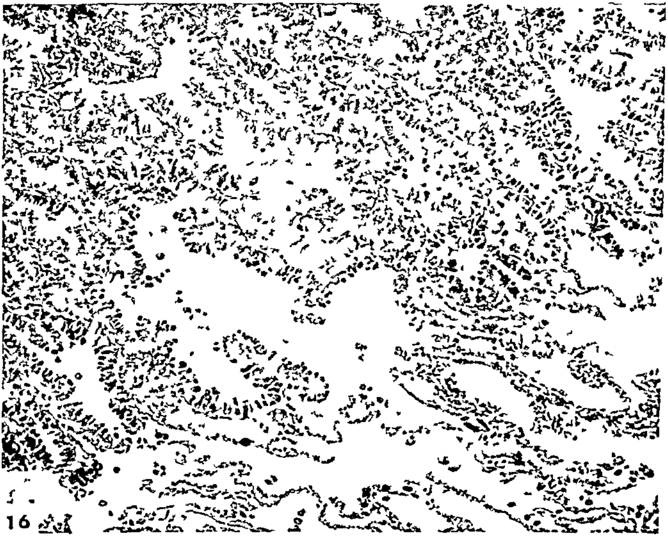
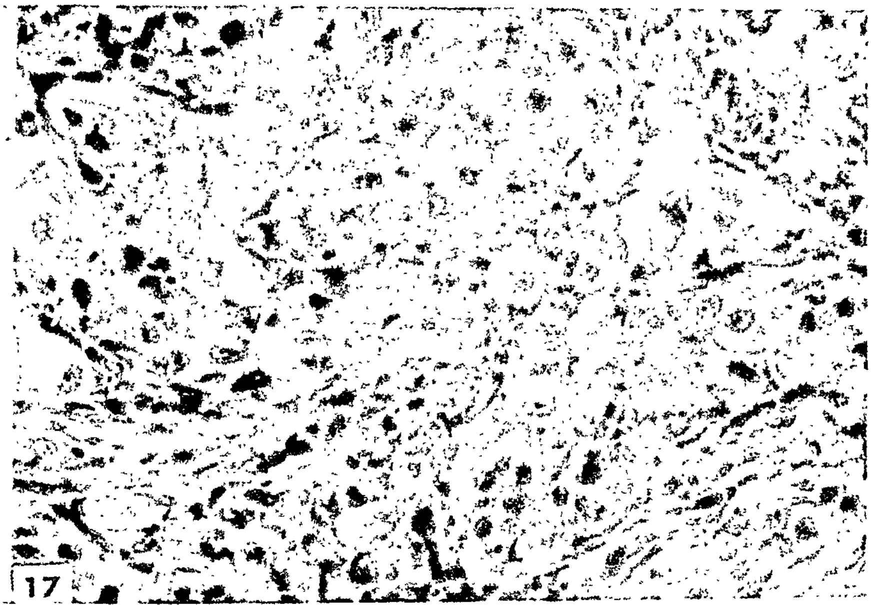


Fig 15.—Case 7 The tumor is composed of thick fibrous septa which are covered by cuboidal nonmucus forming epithelium At the margins the thick septa are continuous with the alveolar septa, but the tumor is well circumscribed The nuclei are irregularly placed in the cells and little cytoplasm is present

Fig 16.—Case 7 At the margins the tumor trabeculae are continuous with the alveolar septa The tumor is circumscribed but not encapsulated

large and the cytoplasm rather scanty. No mucus, cilia, or mitoses were seen. The central portion of the tumor was hyalinized and in this area were numerous large blood vessels and several large cystic bronchioles. Also, in the hyaline area were nests of epithelial cells which tended to form solid sheets of squamous-like cells. These, in places,



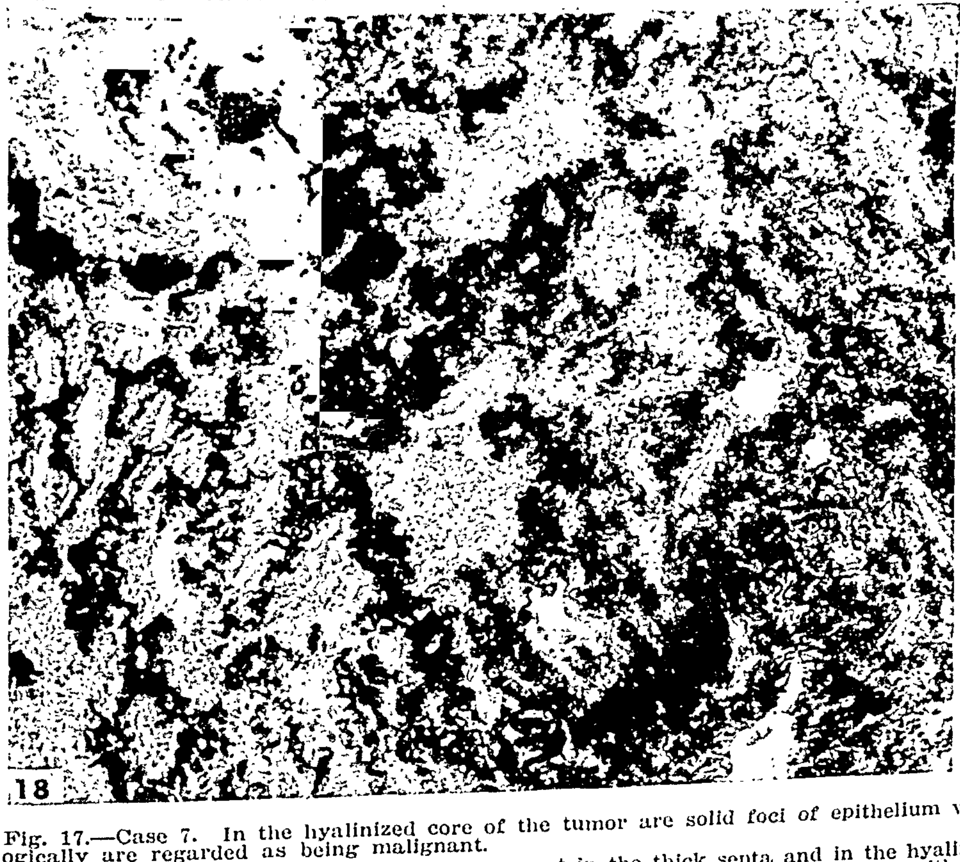


Fig. 17.—Case 7. In the hyalinized core of the tumor are solid foci of epithelium which histologically are regarded as being malignant.

Fig. 18.—Case 7. Many elastic fibers are present in the thick septa and in the hyalinized areas are dense masses of elastic fibers. In this stain (Verhoeff-van Gieson) the epithelium stains faintly.

had the appearance of malignant cells (Fig. 1[illegible]). The tumor extended to the pleura, but did not invade it. In appropriate stains, the trabeculae of the tumor showed an enormous amount of elastic tissue as did the central hyaline core of the tumor (Fig. 18). Numerous sections of the remainder of the lung and the bronchial lymph nodes showed nothing abnormal.

DISCUSSION

The several small tumors found incidentally in autopsies were well circumscribed but not encapsulated single nodules lying beneath the pleura in the peripheral lung fields and were composed of thick fibrous septa covered by a layer of benign appearing cuboidal or nonmucus forming, nonciliated epithelium. In the larger tumors, the centers were hyalinized. The thickened fibrous septa at the margins merged imperceptibly with the alveolar septa and, in appropriate stains, the thickened septa and hyalinized cores were seen to contain large numbers of elastic tissue fibers. These same features characterized the two lesions that became clinically evident and were excised. In these cases, however, the epithelium outside the hyalinized areas was more luxuriant and exactly reproduced the histologic picture of the nonmucus forming type of bronchiolar carcinoma. The photomicrograph used by Liebow[2] to characterize "focal disseminated bronchiolar carcinoma" is certainly similar to our cases. In another paper on this subject, Liebow[3] states that "the lesion may be encountered as a single peripheral focus, as multiple foci, and as an apparently diffuse lesion involving a major portion of a lobe or an entire lobe." Similarly, Watson and Smith,[4] in a discussion entitled, "Terminal Bronchiolar or Alveolar Cell Cancer of the Lung," write the "nodules were discrete and irregular in outline and occasionally had necrotic centers." While they gave no microscopic descriptions the photomicrograph and roentgenogram of their Case No. 21 would lead one to believe it to be similar to our case. Theirs was a small peripheral lesion which produced no symptoms. The 8 month follow up revealed no further disease. Trimble, in a discussion of "coin lesions" of the lung, presented a 3 cm. single bronchiolar tumor similar to our cases. Storey,[6] in a review entitled, "Bronchiolar (Alveolar Cell) Carcinoma of the Lung," briefly presents 3 cases of his own which histologically resemble our cases.

These are examples of localized peripheral lung tumors which can be found in case reports and reviews of alveolar cell carcinoma or bronchiolar carcinoma. Unfortunately these names are used also for another non-bronchogenic or peripheral lung tumor, pulmonary adenomatosis, and its malignant counterpart, alveolar cell carcinoma, in which tall and usually well differentiated mucus secreting columnar cells form a single cell thick membrane lining normal alveolar septa. This disease usually involves extensive areas of the lung, although, in rare instances, it too may present itself as a localized nodule, as in the case reported by Rosemond, Boucot, and Aegerter.[7] The lesion in our Case 5, a 1 cm. subpleural nodule, which was an incidental autopsy finding (see Fig. 5), is another example of a localized single focus of pulmonary adenomatosis. It is our opinion that pulmonary adenomatosis is probably a different disease from that under discussion. Indeed, in reviewing the literature, one gains the impression that several diseases have been loosely grouped under the heading of pulmonary adenomatosis or alveolar cell carcinoma.

The remaining cases of bronchiolar carcinoma, like pulmonary adenomatosis, may involve extensive portions of the lung or may be localized lesions such as just described. Indeed, it may be questioned whether many of these are frankly malignant tumors. It is probable that our cases (6 and 7) are low-grade malignant neoplasms. Others (Cases 1, 2, 3, 4) are undoubtedly benign and have many features of malformations rather than tumors.

These bronchiolar *adenomatous malformations* (Cases 1, 2, 3, 4) bear such a close resemblance to the frankly neoplastic lesions of Cases 6 and 7 that it is difficult not to believe that the tumors arose in similar malformed areas. While it is generally believed that bronchiolar carcinoma arises from bronchiolar epithelium, no theory for their arising in bronchiolar malformations, such as is depicted in Figs. 1 and 2, can be found in the literature. Laipply, Sherrick, and Cape[1] described such an adenomatous nodule which they described as the "smallest bronchiolar adenoma yet described." A close analogy to this possible origin of bronchiolar neoplasms would be the common renal tubular adenomatous malformations which, at times, may be so neoplastic in appearance that they are difficult to distinguish from the malignant renal tumor, hypernephroma. All gradations from the tiny malformations to the malignant hypernephromas exist.[3]

The benign adenomatous bronchiolar malformations, of our cases, are all single lesions, but if the lungs from these autopsied cases had been exhaustively studied, multiple nodules might have been found. Multiple lesions would be a possible explanation for the common widespread nature of bronchiolar carcinoma in the lungs. It is clear that bronchiolar carcinoma in some cases is a localized tumor that is readily curable by surgical excision.

SUMMARY

Four examples of benign bronchiolar tumors are presented which were incidental autopsy findings. The smaller of these lesions (Cases 1 and 2, Figs. 1 and 2) strongly suggest that they are malformations while the larger ones (Cases 3 and 4, Figs. 3 and 4) have characteristics of frank tumor at their periphery, but retain the malformation-like structure centrally. Two successfully surgically treated cases of very slowly growing localized bronchiolar carcinoma are presented (Cases 6 and 7) and their striking similarity to the incidentally found autopsy cases is shown. The new concept that bronchiolar carcinoma may arise from bronchiolar adenomatous malformations, in single or multiple foci, is put forth. The resemblance to the bronchiolar adenomatous malformations in photomicrographs and histologic descriptions of reported cases of bronchiolar carcinoma is discussed. Whether some of the reported cases of bronchiolar carcinoma are indeed malignant neoplasms is questioned.

One example of localized pulmonary adenomatosis, another tumor arising peripherally in the lung, is included (Case 5, Fig 5), only to contrast its histologic picture with the bronchiolar tumors While in the literature, for the most part, pulmonary adenomatosis and its malignant counterpart, alveolar cell carcinoma, are indiscriminately grouped with bronchiolar carcinoma, these two diseases, in our opinion are different in nature and should not be grouped together

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CARCINOSARCOMA OF LUNG OF PERIPHERAL ORIGIN

Charles N. Peabody, M.D., Framingham, Mass.*

This is a case report of an elderly man who was treated for suspected tumor in the mediastinum and who was found to have a carcinosarcoma of the lung. This presentation illustrates the unusual histologic composition of the tumor, its atypical roentgenologic features, and its rare occurrence.

CASE REPORT

This 74-year-old man was admitted to the VA hospital, Providence, R. I., on Jan. 11, 1955, with the chief complaint of daily hemoptysis for the previous 6 weeks. He had slight left chest pain but no weight loss. Past history revealed a cholecystectomy and choledochostomy in 1953, and the smoking of twenty cigarettes a day for "many years." Physical examination revealed diminished breath sounds over the left chest anteriorly, but no râles were heard. Testicles were normal. Blood and urine studies were normal. X-ray studies of the chest disclosed a sharply circumscribed, somewhat lobulated, homogeneous mass, measuring 11 cm. by 9 cm., which extended from the level of the aortic arch down to the hilar region and lay anterior to the trachea, possibly compressing it slightly (Fig. 1). The mass was not present in x-ray studies of May 28, 1953. An intravenous pyelogram was normal. Bronchoscopy revealed a small amount of blood issuing from one of the subdivisions of the left upper main-stem bronchus, probably one of the lingula bronchi. A Papanicolaou smear of the bronchial secretions was consistent with chronic inflammation. Preoperative diagnosis was a malignant tumor of the mediastinum.

On Jan. 24, 1955, an exploratory thoracotomy and left upper lobectomy were carried out. The left lung showed complete development of the major fissure and adherence to the thoracic apex and the mediastinal border. A smooth, lobulated tumor presented in the anterior segmental portion of the upper lobe and appeared to infiltrate the mediastinum, where it was adherent to the phrenic nerve and upper pericardium. It was also adherent to the areolar tissue surrounding the root of the heart. Removal of the tumor necessitated excision of a block of pleura and phrenic nerve. Poor pulmonary reserve in this elderly patient contraindicated total pneumonectomy.

The patient did well following the operation but suffered thrombosis of the popliteal artery of the right leg and underwent a mid-thigh amputation. He was discharged improved on Feb. 23, 1955. However, he returned to the hospital on May 23, 1955, and died of a bleeding duodenal ulcer. At autopsy he was found to have metastasis of this same mixed tumor to retroperitoneal and mesenteric lymph nodes, to liver, to pancreas, and to both kidneys and adrenals. The organ metastases showed both histologic components in every case.

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*Assistant in Surgery, Massachusetts Memorial Hospitals, Boston, Mass.; Visiting Surgeon, Framingham Union Hospital, Framingham, Mass.

Pathologic Study.—

Gross examination: The left upper lobe and its tumor weighed 260 grams. The rounded mass was 8 cm. in diameter. When the lung was incised, a large solid tumor rolled out of the lung revealing a cavity lined by a shaggy membrane, 0.2 cm. thick. On section, the tumor was wet, friable, and gray with alternating dark red zones of hemorrhage. Dissection of the bronchi to the fifth order in all directions revealed no evidence that the tumor arose from the opened lumina. Nine intrapulmonary nodes were found, the largest of which was 1 cm. in diameter.

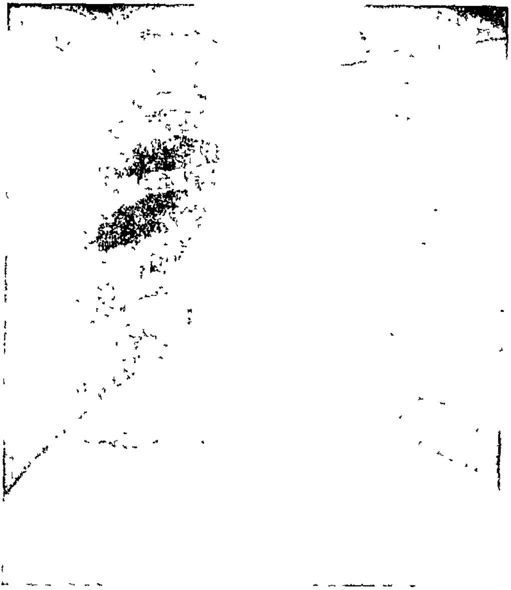

Fig. 1.—This posteroanterior roentgenogram shows the smooth peripheral border of the tumor which on lateral films was seen to be in the anterior superior mediastinum.

Microscopic examination: Multiple sections revealed a malignant neoplasm composed of cells of two distinct histologic types. Type A showed an epithelial component of atypical polyhedral and low columnar cells forming large and small irregular glands, often with papillary arrangement. The carcinoma cell type strongly suggested peripheral (alveolar) origin. The individual cell of Type A had a large oval nucleus with coarse granular chromatin and violet cytoplasm. Type B was a malignant mesenchymal tumor which Gomori's trichrome and Laidlaw's reticulum stains identified as fibrosarcomatous with a delicate reticulum pattern surrounding the individual spindle cells. The cells of Type B were long and fusiform, irregular, with granular nuclei and blue cytoplasm but were not as deeply colored as the cells in Type A. Numerous mitoses were seen in both components. Throughout the stroma were areas of necrosis and hemorrhage. No tumor was seen in the lymph nodes and the tumor had not invaded its "capsule." Final diagnosis: Malignant mixed tumor of the lung with adenocarcinomatous and fibrosarcomatous components.

DISCUSSION

According to Willis,[6] a carcinosarcoma in a neoplasm of epithelial and non-epithelial cells or an epithelial neoplasm with sarcomatous degeneration of its stroma. It is not to be confused with the "collision tumor" which is an accidental growth of a sarcoma and carcinoma next to one another. Multiple section examination will reveal there is no free intermingling of components as is seen in the carcinosarcoma. Bergmann, Ackerman, and Kemler,[1] state that carcinosarcoma of the lung is rare since they were able to find mention of only 8 other cases in the literature. The histologic feature of our tumor differs slightly from the cases reported by Bergmann and his associates. The carcinomatous elements in the two tumors he studied were epidermoid in differentiation. Frank[2] reports a 45-year-old man who had a large lesion in the left lower lobe with metastasis to the heart, stomach, duodenum, and kidney. At autopsy,

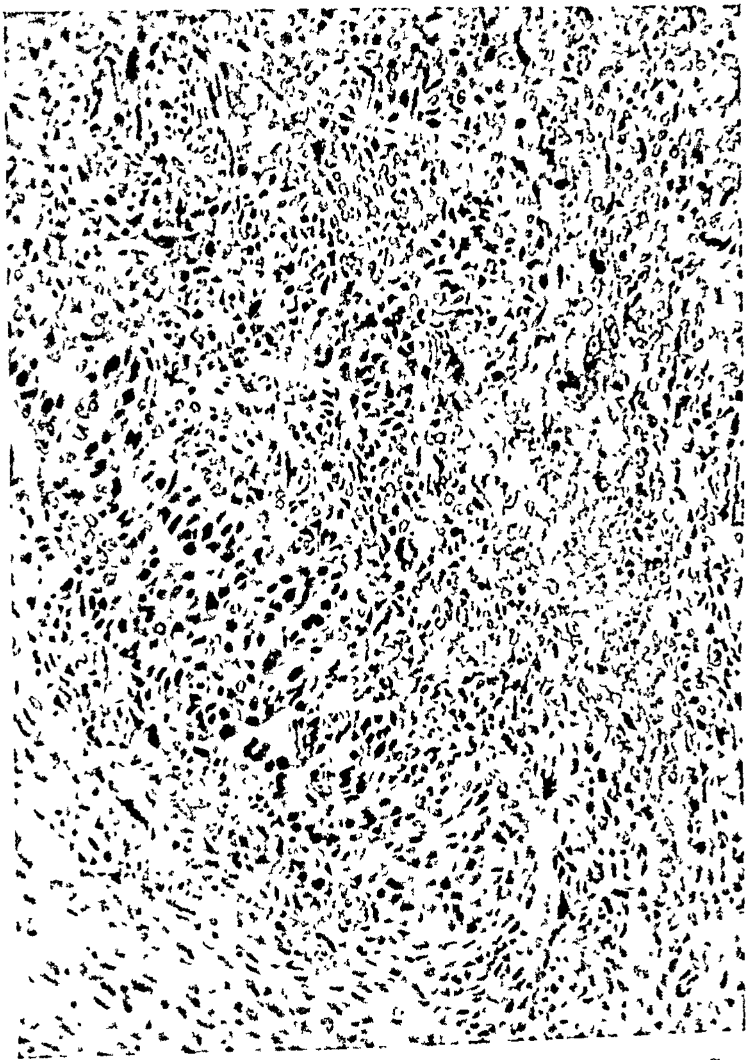

Fig. 2.—This photomicrograph, taken of the tumor tissue stained by Gomori's trichrome method, shows the intermingling carcinoma cells in gland pattern and the atypical fibrosarcoma cells. (× 125; reduced ⅕.)

the tumor had an adenopapillary pattern in the carcinomatous element and spindle cells in the sarcomatous component. Ogawa[4] reports a 70-year-old man who died with a lesion in the right upper lobe without metastasis. Microscopy revealed that the carcinomatous component was adenocarcinoma with transitional cells. The sarcoma was composed of spindle cells. Weber[5] describes a 77-year-old man with a large left upper lobe tumor which had metastasized to hilar and mesenteric lymph nodes, brain, adrenal, kidney, stomach, and jejunum. Histologic examination revealed epidermoid, adenocarcinomatous, and undifferentiated carcinoma in it, as well as spindle cell sarcoma. All authors report that a carcinosarcoma may metastasize as a sarcoma, as a carcinoma, or as both. The gross features of this case also differ from the cases reported by Bergmann which were of pedunculated intrabronchial tumors. Our lesion was not associated with a major bronchus and was probably of bronchiolar origin. The 2 patients reported by Bergmann were alive without evidence

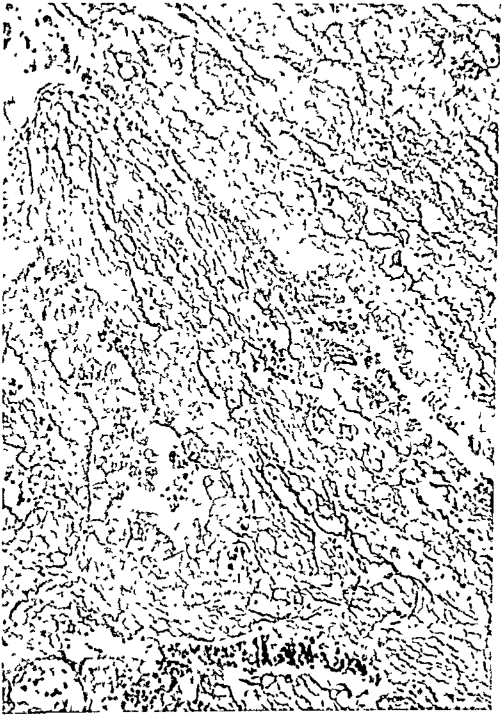

Fig. 3—The same tissue sections stained with Laidlaw's reticulum show the fine pattern of reticulum seen in fibrosarcoma. (× 125, reduced ⅕.)

of recurrence at 6 years and at 1½ years, respectively, after total pneumonectomy. The other cases mentioned in literature were based on autopsy findings. Liebow[3] suggests that carcinosarcomas of lung may represent epidermoid tumors manifesting a tendency toward extreme pleomorphism. Our positive reticulum stain does not support his view.

Willis reviews some experimental work concerning the origin of carcinosarcoma and suggests that a mother cell may give rise to both carcinoma and sarcoma in the same tumors in animals, and perhaps human origin is on the same basis. He points out that apparent sarcomatous changes may take place in a carcinoma successively transplanted in animals. He likewise notes that certain chemical carcinogens have been said to produce tumors of both sarcomatous and carcinomatous constituents.

SUMMARY

A case is reported of an elderly man who underwent left upper lobectomy for a tumor in the chest resembling a mediastinal mass. The tumor proved to be a carcinosarcoma of the lung, with adenocarcinomatous and fibrosarcomatous components. At autopsy, 5 months after lobectomy, metastases containing both histologic components were found in retroperitoneal and mesenteric lymph nodes, in liver, pancreas, both kidneys, and both adrenals. This is the eleventh carcinosarcoma of the lung (and the first of peripheral origin) reported in the literature.

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LUNG CANCER—METASTATIC THEORY AND SURGICAL PRACTICE

W. I. B. Onuigbo, M.B. (Glas.), B.Sc. (Lond.), Glasgow, Scotland*

IN SURGERY for lung cancer, there is need for the surgeon "to better his technique and the efficiency of his curative operations" (Brock[3]). In this connection, it is agreed that lymph nodes should be excised but to date there is no general agreement on how far to go. Thus, while Watson[12] wanted "a radical pneumonectomy which removes all possible lymphatic areas," Delarue[4] deprecated "a direct surgical attack on ipsilateral mediastinal lymph nodes."

Hayward[6] has suggested that the surgery of lung cancer "would be far more securely established if it could be shown to rest on sound pathological principles." For example, is radical pneumonectomy justified on pathologic grounds? It was the late Archibald Leitch who pointed out that radical operations should be based on numerous pathologic studies aimed at discovering metastatic routes. The present paper fulfills this objective by bringing together studies that I have carried out on metastatic pathways in bronchogenic carcinoma. It justifies radical pneumonectomy.

INVESTIGATIONS

Statistical analysis of 1,000 necropsy records of lung cancer collected from Glasgow hospitals showed a significant involvement of the ipsilateral adrenal (Onuigbo[8]). The value of χ^2 was 8.4, p being less than 0.005. In cases showing bilateral adrenal metastases, the ipsilateral deposit was usually larger than the contralateral. Out of 184 cases, in which bilateral deposits were fully described, there were larger ipsilateral deposits in 121 and larger contralateral growths in only 63 (Onuigbo[10]). This ipsilateral preponderance is highly significant.

Of 115 bronchial carcinomas metastasizing to the liver, 77 gave rise to deposits confined to, or predominating in, the ipsilateral lobe, only 38 cases showed a contralateral tendency (Onuigbo[9]). This ipsilateral trend is significant ($\chi^2 = 13.26$, $p < 0.001$).

On analyzing 260 bronchial carcinomas invading the kidneys (Onuigbo[10]), I found that 150 showed deposits which were either ipsilateral or larger ipsilaterally, as against 110 showing a contralateral trend. This finding is also significant ($\chi^2 = 6.15$, $p < 0.025$).

From the Department of Pathology, The University and Western Infirmary, Glasgow, Scotland.

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*Present address: General Hospital, Enugu, Nigeria.

of recurrence at 6 years and at 1½ years, respectively, after total pneumonectomy. The other cases mentioned in literature were based on autopsy findings. Liebow[3] suggests that carcinosarcomas of lung may represent epidermoid tumors manifesting a tendency toward extreme pleomorphism. Our positive reticulum stain does not support his view.

Willis reviews some experimental work concerning the origin of carcinosarcoma and suggests that a mother cell may give rise to both carcinoma and sarcoma in the same tumors in animals, and perhaps human origin is on the same basis. He points out that apparent sarcomatous changes may take place in a carcinoma successively transplanted in animals. He likewise notes that certain chemical carcinogens have been said to produce tumors of both sarcomatous and carcinomatous constituents.

SUMMARY

A case is reported of an elderly man who underwent left upper lobectomy for a tumor in the chest resembling a mediastinal mass. The tumor proved to be a carcinosarcoma of the lung, with adenocarcinomatous and fibrosarcomatous components. At autopsy, 5 months after lobectomy, metastases containing both histologic components were found in retroperitoneal and mesenteric lymph nodes, in liver, pancreas, both kidneys, and both adrenals. This is the eleventh carcinosarcoma of the lung (and the first of peripheral origin) reported in the literature.

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LUNG CANCER—METASTATIC THEORY AND SURGICAL PRACTICE

W. I. B. Onuigbo, M.B. (Glas.) B.Sc. (Lond.), Glasgow, Scotland*

IN SURGERY for lung cancer, there is need for the surgeon "to better his technique and the efficiency of his curative operations" (Brock[3]). In this connection, it is agreed that lymph nodes should be excised but to date there is no general agreement on how far to go. Thus, while Watson[12] wanted "a radical pneumonectomy which removes all possible lymphatic areas," Delarue[4] deprecated "a direct surgical attack on ipsilateral mediastinal lymph nodes."

Hayward has suggested that the surgery of lung cancer "would be far more securely established if it could be shown to rest on sound pathological principles." For example, is radical pneumonectomy justified on pathologic grounds? It was the late Archibald Leitch who pointed out that radical operations should be based on numerous pathologic studies aimed at discovering metastatic routes. The present paper fulfills this objective by bringing together studies that I have carried out on metastatic pathways in bronchogenic carcinoma. It justifies radical pneumonectomy.

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Of 115 bronchial carcinomas metastasizing to the liver, 77 gave rise to deposits confined to, or predominating in, the ipsilateral lobe, only 38 cases showed a contralateral tendency (Onuigbo[9]). This ipsilateral trend is significant ($\chi^2 = 13.26$, $p < 0.001$).

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From the Department of Pathology, The University and Western Infirmary, Glasgow, Scotland.

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*Present address: General Hospital, Enugu, Nigeria.

A collateral study on the brain also showed a significant ipsilateral disposition with respect to the metastatic involvement of the cerebral and cerebellar hemisphere—$\chi^2 = 5.02$, $p = 0.025$ (Onuigbo[11]). Fifty-five cases collected from the literature gave a comparable result.

DISCUSSION

In cancer surgery, according to Allison,[1] "rough generalizations are possible and are clinically helpful." Since radical pneumonectomy requires excision of all ipsilateral lymphatic tissue, it is helpful to be able to generalize that lung cancer spreads ipsilaterally. My topographical studies are in accord with this generalization. Lymph node invasion is also largely ipsilateral (Onuigbo[8]).

These observations suggest that, in the genesis of visceral metastases, lymphatic carriage of cancer cells is a probability. In consequence, since ipsilateral lymphatic tissue in the chest is the logical halfway station for such distant metastases, the desirability of radical clearance of all such tissue at pneumonectomy would seem to be indicated.

Long ago, Arnott[2] noted that the zeal and hopefulness of a surgeon depended "in a great measure upon the particular theory which he may hold." Handley[5] was of the opinion that the hematogenous theory of metastasis has "remained as a direct discouragement to the surgeon's efforts." Fortunately, as shown above, this need not be, for a lymphogenous theory is possible. This theory in principle justifies the operation of radical pneumonectomy for lung cancer.

CONCLUSION

Early diagnosis and adequate surgery can change the dim outlook in lung cancer. Radical excision of ipsilateral lymphatics is not yet generally accepted as the treatment of choice in this fell disease. It is, however, a sound procedure for topographical pathology suggests that lung cancer exhibits a statistically significant bias toward invading ipsilateral lymph nodes, adrenal, kidney, hepatic lobe, cerebral and cerebellar hemispheres. If the patient's condition allows it, prophylactic dissection of all lymphatic tissue in the hemithorax is indicated.

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OBSERVATIONS ON PULMONARY VASOMOTOR REFLEXES

Paul W. Sanger, M.D., Francis Robicsek, M.D., Frederick H. Taylor, M.D., Roberto Magistro, M.D., and Egidio Foti, M.D., Charlotte, N. C.

PULMONARY hypertension is a frequent companion of various cardiopulmonary diseases. Many operations have been performed with the aim of curing or preventing this complication; still the basic physiologic problems of pulmonary hypertension are far from being solved.

Many years go, primary pressure elevation in the left atrium and pulmonary veins was cited as an explanation for pulmonary hypertension in mitral stenosis and in left ventricular failure. It has been generally accepted also that increased pulmonary flow alone may be responsible for the development of pulmonary hypertension in certain cases of congenital heart disease.

Progress in circulatory research introduced by heart catheterization has shown the problem of pulmonary hypertension is more complex than previously supposed. Interest has been focused on special functional problems of the lesser circulation, primarily the role played by the small pulmonary vessels in the regulation of blood pressure in the lungs.

The relationship between pulmonary hypertension and anatomic changes in the small pulmonary vessels in different cardiopulmonary conditions has been investigated extensively and described in detail.[1-7] The circumstances affecting the functional changes which precede or accompany anatomic changes differ. There is considerable controversy regarding vasomotor control of the pulmonary circulation. Some investigators[8-10] deny even the existence of vessels in the lung capable of vasoconstriction, but others[11-51] believe that pulmonary vascular reflexes deeply affect the clinical picture, limit the surgical operability, and influence the postoperative results.

It has been asserted[16, 21, 24, 25, 37, 43] that elevation of the left atrial and pulmonary venous pressures causes a great increase in pulmonary arterial pressure in conditions where the pulmonary capillary pressure approaches the colloidal osmotic pressure of blood. Dexter and his associates[22] have suggested that this elevation of pulmonary arterial pressure might be due to a reflex arteriolar vasoconstriction. They also proposed that an increase in the pulmonary arteriolar resistance ("precapillary barrier") may protect the capillary bed of the lungs from a sudden surge of blood from a competent

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right ventricle, thus preventing the development of pulmonary edema. This theory was supported by clinical observations[14, 17, 27, 30, 32, 39, 40, 44, 47, 50] that abnormally high pulmonary arteriolar resistance may be decreased by the administration of ganglion blocking agents or by performing a successful mitral commissurotomy.

The concept concerning pulmonary reflex vasospasm has been challenged recently.

1. Some authors state that they were unable to find an increase in pulmonary arteriolar resistance following exercise in patients with mitral stenosis.[52]
2. Others contended that the effect of ganglion blocking agents is due to systemic vasodilatation and "pooling of the blood" rather than to pulmonary arteriolar dilatation.[26, 41, 51]
3. Finally, other investigators found that elevation of left atrial and pulmonary venous pressures was followed by an immediate decrease in pulmonary arteriolar resistance, which is in complete disagreement with the reflex theory.[15, 18, 53]

Because of the controversy, we thought it reasonable to investigate the problem of pulmonary vasomotor response by elevating the pulmonary venous pressure experimentally, where this effect could be selectively studied.

MATERIALS AND METHODS

Mongrel dogs, weighing from 10 to 20 Kg., were used. They were anesthetized by sodium Pentothal and intubated endotracheally. Ventilation was maintained with a Jefferson respirator. A left anterolateral thoracotomy was performed in the fourth interspace. The hilus of the lung was cautiously dissected and care was taken to avoid injury to the hilar and perivascular nerve fibers. Ligatures were placed around the left pulmonary artery and veins and the left main bronchus was isolated and occluded. Leaving the nervous connections intact, the left lung was excluded from ventilation and pulmonary circulation.

The veins of the isolated left lung were cannulated with polyethylene tubes. These tubes were brought through the chest wall as the thoracotomy incision was closed, and the pleural cavity was drained through an intercostal catheter placed under 4 cm. of water. Thereafter, spontaneous respiration was restored.

Then normal saline (in some of the experiments whole blood) was infused through the polyethylene tubes. In this way the pressure in the veins and capillary system of the isolated left lung was elevated to 35 to 45 mm. Hg without directly altering the hemodynamics of the intact right lung or the systemic circulation.

In the course of the experiments, pressure was measured continuously in the right pulmonary artery, left atrium, femoral artery, inferior vena cava, left pleural cavity, and in the veins of the isolated left lung. The mean pressure was determined by electronic integration. The ventilation and oxygen uptake were measured bronchospirometrically. Blood samples were taken from the right pulmonary artery and from the left atrium. The oxygen content of these samples was determined photometrically.

The blood flow through the right lung and systemic vessels was calculated by the Fick principle. Pulmonary arteriolar resistance was calculated and expressed in dynes per centimeter per second^{-5} units by dividing the pulmonary artery-left atrium pressure gradient by the pulmonary blood flow.

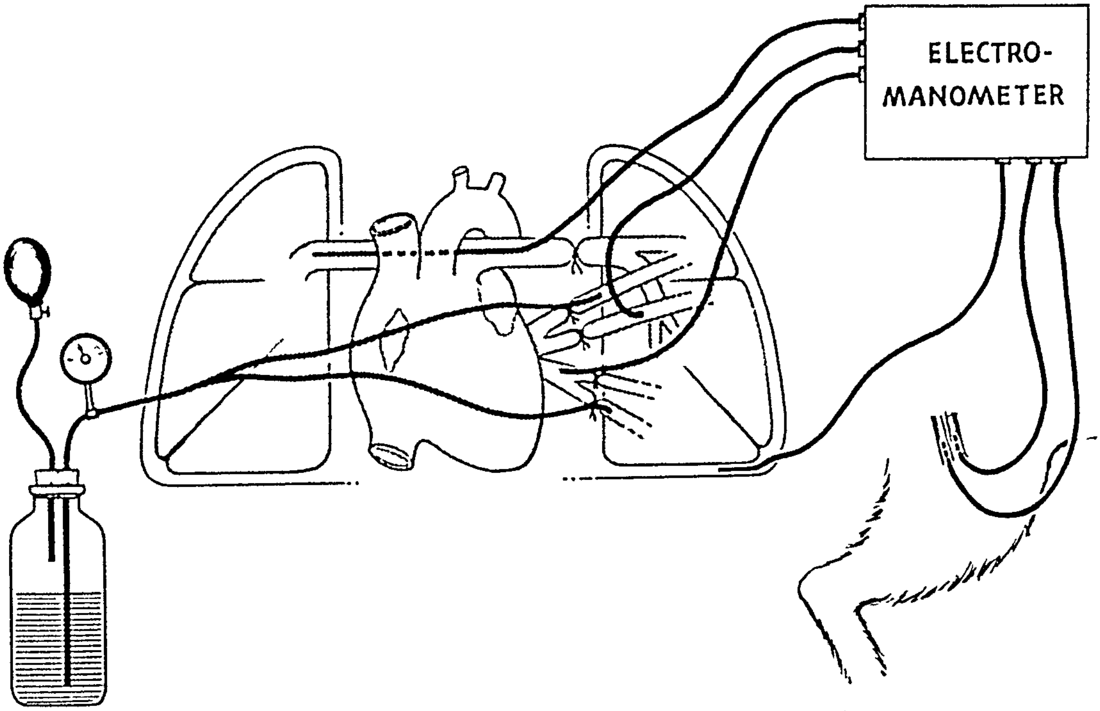

Fig. 1.—Schematic representation of the experiment.

Rhodanate dye was infused in 5 experiments, and the "escaped" volume through the bronchial vessels and lymphatics was determined.

In a control series of experiments, a right thoracotomy was performed under aseptic conditions. The entire right thoracic sympathetic chain was extirpated from the stellate ganglion to the diaphragm. The vagus nerve was dissected free and all its thoracic branches were severed. The chest was closed thereafter in the usual manner. Fourteen to 16 days following this operation a left thoracic sympathectomy with transsection of the thoracic vagus branches was done. The procedure otherwise (isolation of the left lung, etc.) was identical to that described in the first series.

RESULTS

Thirty experiments were performed in the first series and 10 in the second (control) group. A summary of the results derived from these experiments follows.

Abnormally increased pressure in the venous and capillary system of the isolated lung did not alter generally the systemic circulation. The arterial and venous pressures remained the same. The cardiac output increased more than 30 per cent only in 3 and decreased in 7 cases. There was no significant change in the systemic circulatory resistance, arterial oxygen saturation, or arteriovenous oxygen difference. The left atrial pressure remained stabile.

In most of the experiments, the infusion was followed by a moderate increase in the respiratory rate without a significant alteration of the minute ventilation or oxygen uptake.

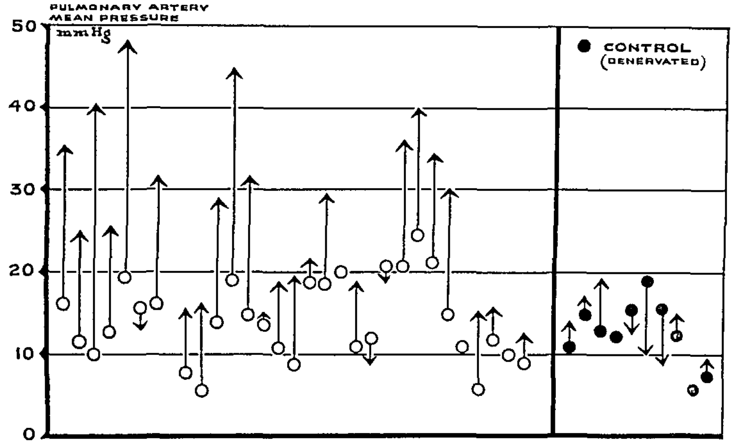

Fig. 2.—Changes in pulmonary arterial pressure after high pressure infusion.

Unlike the systemic circuit, the hemodynamics of the intact right lung changed profoundly. In 30 cases, the pulmonary arterial pressure rose significantly in 20 cases, slightly in 4, decreased moderately in 3, and remained the same in 3. In most of the cases, the pulmonary arteriolar resistance rose sharply, indicating arteriolar vasoconstriction. In 16 cases this elevation exceeded 100 per cent of the basal values. This elevation of the arteriolar resistance became *manifest primarily in the elevation of the pulmonary arterial* pressure and not in the decrease of the pulmonary blood flow.

In 10 control cases where bilateral thoracic sympathectomy and transsection of the pulmonary vagus branches preceded the experiment, the above changes in pulmonary hemodynamics did not develop. The pulmonary arterial pressure elevated moderately only in 1 case (6 mm Hg), slightly in 5, and remained the same or decreased moderately in 5 cases. We were unable to observe significant elevation in the pulmonary arteriolar resistance (more than 30 per cent) in any of the control animals.

In 5 experiments, where rhodanate was added to the infusion, the "escaped" fluid *volume was estimated and found to be negligible (less than* 40 ml in an observation period of 20 minutes).

DISCUSSION

In the experiments described, normal saline solution or blood was infused under pressure into the isolated left lung. The most important circulatory event observed in the course of the infusion was the acute development of pulmonary hypertension in the intact right lung. This may have different explanations.

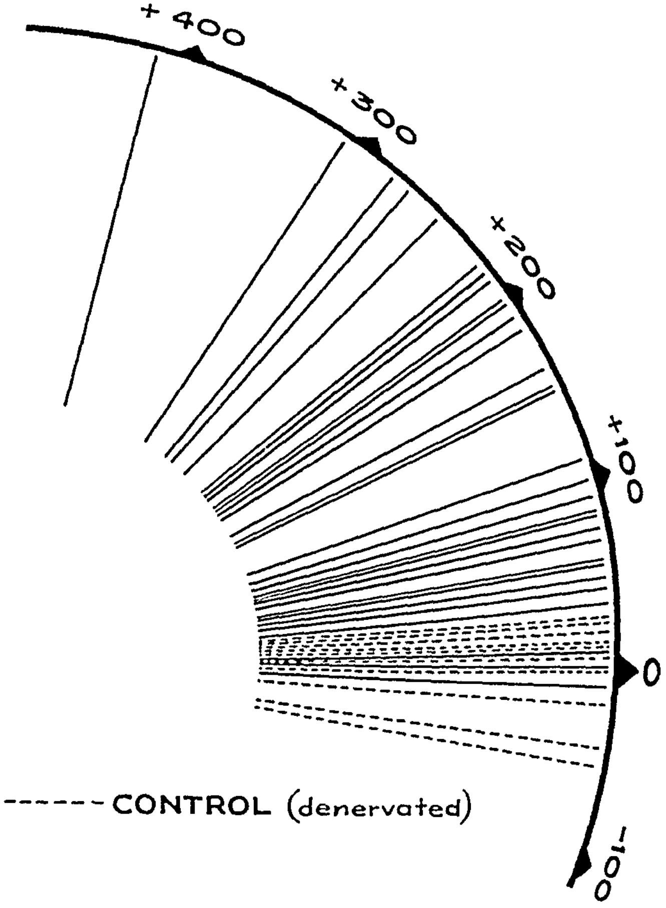

Fig. 3.—Changes in pulmonary "vascular" circulatory resistance after high pressure infusion (expressed in per cent of the basal values).

One such explanation is that the left lung was isolated from the pulmonary but not from the bronchial or lymphatic circulations, and part of the infused fluid escaped through these vessels, increasing acutely the circulating blood volume. This hypervolemia may lead to the development of pulmonary hypertension in animals having undergone a physiologic left pneumonectomy.

Our experimental observations proved that such hypervolemia could not account for the increase in pulmonary arterial blood pressure.

1. In 27 out of 30 cases the cardiac output remained the same or even decreased, indicating that the pressure elevation was due to an increase in circulatory resistance and not to an increase of pulmonary blood flow.

2 Systemic venous and left atrial blood pressures also remained stable

3 Furthermore, the rhodanate dye determinations gave evidence that the "escaped" volume did not exceed 20 to 40 ml, which is negligible

4 Finally, our experiments showed that this pulmonary arterial pressure elevation was not due to an increase in intrathoracic pressure

The increase of the pulmonary artery left atrium pressure gradient with stabile pulmonary blood flow proves that the pulmonary hypertension was a consequence of an active constriction of smaller pulmonary vessels probably the arterioles Similar effect was demonstrated by van Bogaert[18] and Denny Brown[50] and their associates on cerebral circulation

The fact that the above changes of the pulmonary hemodynamics did not occur following bilateral thoracic sympathectomy and resection of the thoracic vagus branches supports the theory that the elevation in pulmonary vascular circulatory resistance is nervous in origin This is in accordance with reflex concept, namely, that elevated pulmonary venous and capillary pressure induces an arteriolar spasm in the lungs

Our experiments do not give information as to the exact localization of the pressoreceptors or the detailed pathway of this reflex, however observations made by Duken,[29] Wiggers[57] and their co workers indicate that the pulmonary vasoconstrictor fibers run primarily through the sympathetic system

Finally, the question arises, "What is the clinical importance of this reflex activity?" Dexter supposes that the vasospasm is a compensatory phenomenon, and the arteriolar narrowing leads to a further elevation of pulmonary arterial presssure, as precapillary barrier it protects the most vulnerable part of the pulmonary vascular bed On the basis of our experiments, we are not able to prove or disprove this conclusion, primarily because our observations were made on healthy animals and not on human beings with heart disease, but comparing the results of our experiments with clinical observations it is our impression that the reflex arteriolar vasomotor activity plays an important role in the regulation of pulmonary circulation As any other functional vasoconstriction existing for a prolonged period of time, the spasm of pulmonary arterioles too will sooner or later give rise to organic vascular changes

SUMMARY

There is considerable controversy in medical literature regarding the vasomotor control of pulmonary vessels The authors studied experimentally the significance of pulmonary reflex vasospasm in the development of pulmonary hypertension

The left lung was isolated from pulmonary circulation and ventilation The nervous connections were left intact The pressure was elevated in the venous and capillary system of the isolated left lung by high pressure infusion This pressure elevation was immediately followed by pulmonary hypertension and arteriolar constriction in the opposite intact lung

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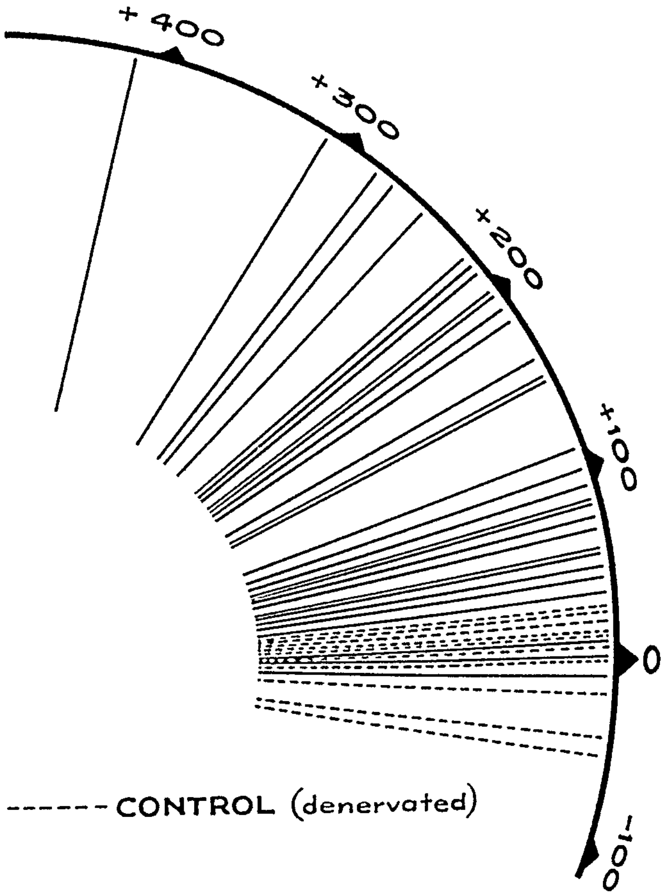

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These experimental observations prove that elevation in pulmonary venous and capillary pressure causes arteriolar vasospasm in the lungs, and this reflex plays an important role in the regulation of the lesser circulation.

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BILATERAL EXTRAPERIOSTEAL PARAFFIN PLOMBAGE FOR PULMONARY TUBERCULOSIS

R. T. Fox, M.D., Wm. M. Lees, M.D.,** T. W. Shields, M.D.,****
*E. DiMarco, M.D.,**** and N. Manzo, M.D.,**** Chicago, Ill.*

DESPITE better case finding methods and improved chemotherapy for active tuberculosis, the patient with extensive bilateral pulmonary tuberculosis is still a major problem. The majority of patients with such involvement can be be brought under control and the disease arrested by chemotherapy alone. An additional group will achieve sufficient improvement so that resection of the significant residual lesions may be accomplished safely by unilateral or bilateral procedures. In the remaining minority in whom the residual disease is so extensive or the pulmonary reserve so low that resection is extremely risky if not impossible, bilateral surgical collapse is often feasible. We should like to present our experience with a group of such patients who have been treated with bilateral thoracoplasty with extraperiosteal paraffin plombage.

A review of the literature shows that a bilateral approach in the treatment of pulmonary tuberculosis has run the gamut from Forlanini in 1911[1] to F. J. Lewis and his associates in 1954. Only when lung transplants or artificial lungs are available can one become more radical. Forlanini advocated the use of bilateral pneumothorax, successively applied rather than simultaneously. In 1912, Ascoli[1] *recommended simultaneous bilateral pneumothorax and others fol*lowed this lead in subsequent years. Curti[1] in 1927 reported the use of bilateral phrenic neurectomy. In 1929, Anneuille[1] and also Maendl[1] published an account of patients in whom pneumothorax and contralateral thoracoplasty were used successfully. Kinsella,[3] in 1930, reported a series of dogs and monkeys in which bilateral thoracoplasty was well tolerated. It was not until 1932 that any reports of bilateral thoracoplasty in human beings were published. Duff Allen,[1] Jessen,[4] and Gravesen[5] each reported a single case of partial bilateral thoracoplasty, performed as staged procedures, and apparently tolerated well by the patients. These and other authors also discussed the use of thoracoplasty

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*Assistant Chief of Surgery, Municipal Tuberculosis Sanitarium, Chicago, Ill., and Associate in Surgery, Northwestern University Medical School.

**Chief of Surgery, Municipal Tuberculosis Sanitarium, Chicago, Ill., and Clinical Associate Professor in Surgery, Loyola University Stritch School of Medicine and Mercy Hospital.

***Attending Thoracic Surgeon, Veterans Administration Research Hospital, Chicago, Ill., and Associate in Surgery, Northwestern University Medical School.

****Formerly Resident in Surgery, Municipal Tuberculosis Sanitarium, Chicago, Ill.

with contralateral procedures of lesser magnitude such as extrapleural pneumonolysis, with or without plombage. In the ensuing two decades, various authors throughout the world reported cases of bilateral thoracoplasty: Magri,[6] Finochietto,[7] Coryllos and Ornstein,[8] Netto,[9] Roger and Lemieux,[10] Meltzer,[11] Samuel,[12] Paulino and Loureiro,[13] Seip,[14] Kano,[15] Lund,[16] and Beaconsfield and co-workers.[17]

In 1950, reports of the use of extraperiosteal plombage procedures began to appear.[18, 22, 23, 25, 26, 27] In 1953, Povah[19] reported 4 patients in whom bilateral extraperiosteal Lucite ball plombage had been performed. In the same year, Woods and Buente[20] published a series of 285 cases of extraperiosteal Lucite ball plombage, 15 of which were bilateral.

In 1952 and 1953, reports of bilateral resections for pulmonary tuberculosis began to appear in the literature, and the results have been excellent. Shumway, Lewis and their associates,[2] in 1954, and again in 1956,[21] reported a series of patients in whom simultaneous bilateral resections were successfully performed. Certainly the brilliant results reported from clinics throughout the world demonstrate that resection of significant residual tuberculous disease is the procedure of choice when this can be done adequately and with reasonable safety.

At the Chicago Municipal Tuberculosis Sanitarium, during the years 1951 through 1957, 46 patients have had bilateral thoracoplasty performed with extraperiosteal paraffin plombage and our experience with these patients is the basis of this report. During this 7-year period, a total of 760 extraperiosteal plombage procedures has been performed. In the same period, 1,040 pulmonary resections were done, 54 of which were bilateral. Our ratio of resection versus collapse has changed markedly in this period, the present ratio being five to one in favor of resection.

TECHNIQUE

The technique of the plombage operation has been reported elsewhere,[26, 27] and differs only in detail from that done in other clinics. Usually a short posterior portion of the third or third and fourth ribs is resected, and then a space created by subperiosteal stripping of ribs 1 and 2 and also 5 and even 6, 7 or 8 if necessary, depending on the extent of the disease. The paraffin is molded into this space loosely while it is still warm enough to be malleable. No polyethylene bag or other plastic material has been used by us. There is a peculiar foreign body reaction to the paraffin that occurs in a moderate percentage of patients. This consists of a softening of the outer surface of the paraffin pack and subsequent extrusion through a small defect in the "capsule" into the soft tissues of the chest wall. This may occur at any interval from 6 months to several years, and usually necessitates removal of the pack. This removal is a simple procedure, rarely followed by any significant re-expansion of the underlying lung. In this series of 46 patients, 16 paraffin packs have been removed or 17.4 per cent of the 92 packs inserted.

INDICATIONS

In general, the indication for surgery was bilateral cavitary disease or extensive infiltrative disease persisting after 6 months or more of adequate rest and antituberculous chemotherapy—usually a combination of streptomycin, PAS, and INH Resection, of course is the procedure of choice, but in many patients there are at least relative contraindications to resection and these make up the indications for collapse In this group are the following (1) those patients whose significant residual disease is so widely distributed as to make adequate resection impossible, (2) patients who have persistent endobronchitis which fails to respond to treatment, (3) some patients whose sputum is still positive and whose organisms have been demonstrated or assumed to be resistant to all available antibiotics, and (4) those patients whose physiologic age, impaired respiratory reserve, or poor general condition put them into the high-risk group as far as resection is concerned All the published reports on resectional surgery have demonstrated that the great percentage of complications and deaths occurs in patients falling into one or more of the above categories

The 46 patients ranged in age from 17 to 63 years, one half were under 40 and half over 40 There were 29 men and 17 women, 29 were white, 16 Negro, and 1 Oriental All but 3 were classified as far advanced, the others fitting the NTA classification of moderately advanced All but one had bilateral cavitation demonstrated roentgenographically All had been treated with varying combinations of antituberculous agents—the earlier patients in the series having had short term interrupted courses as was the practice at that time Thirty four had received pneumoperitoneum as part of their medical treatment The poor response of these patients to treatment is reflected in the duration of the treatment prior to the surgery Only 8 patients were operated upon less than one year after initiation of medical treatment Thirty five had from one to 2 years of treatment, and 3 had more than 2 years Even after all this treatment, 18 patients had positive sputum preoperatively Seventeen had tuberculous endobronchitis diagnosed bronchoscopically at some time during their medical treatment In most of these, the bronchial disease cleared on subsequent examination

COMPLICATIONS

There was no mortality in any of these 46 patients (92 operations) The *only complications were minor and in no instance altered the patient's surgical* result or long range prognosis In 5 operations, the parietal pleura was inadvertently torn This was handled by needle or catheter aspiration during the closure Subsequent films showed no residual pneumothorax or significant effusion *In 4 patients there was sufficient collection of serous fluid around the* paraffin pack to warrant aspiration This was only a transient problem One patient developed a large hematoma of the chest wall requiring evacuation There was no instance of wound infection, spread of disease, atelectasis, or even significant dyspnea in any of these patients

RESULTS

Of the 46 patients, all but 3 left the sanitarium. One patient died 4 months postoperatively of a brain tumor; his pulmonary disease was controlled. Another died in the sanitarium 18 months postoperatively with cor pulmonale. His sputum had been negative for one year before death. The third patient remains in the sanitarium 18 months postoperative, with his disease still active and the sputum positive.

Thirty-five patients were given regular discharges, either with "inactive" status or "active improved, with good prognosis." Of these 35 patients, one has died of her tuberculosis, 2 have died of nontuberculous causes, and one still has active disease although sputum cultures are currently negative. Three patients, with persistent cavitation, were given "Maximum Hospital Benefit" discharges. Patients discharged in his category still have active disease with or without cavitation and with or without positive sputum cultures. None is discharged with positive sputum concentrates. They are either deemed unfit candidates for further surgery or have refused recommendation for reoperation. Two of these 3 patients have since died of their tuberculous disease, and one is alive, but still has active disease. The remaining 5 patients had irregular discharges, i.e., they left against advice. Of these 5 patients, 2 are well (inactive) and working, one has active disease, and 2 have been lost to follow-up. One patient had a subsequent pulmonary resection after the bilateral plombage. She is well today. The minimum follow-up period of this group is one year, and 40 (87 per cent) have been followed more than 2 years.

The present status of all the patients, with a follow-up of one to 7 years is as follows: 32 (70 per cent) are alive, "inactive" and working; 1 (2.1 per cent) is alive and "inactive" but is physically unable to work due to progressive emphysema with cor pulmonale; 4 (8.6 per cent) are living with active disease (1 is still in the sanitarium); 3 (6.4 per cent) have died of tuberculosis; 4 (8.6 per cent) have died of nontuberculous causes, but their tuberculosis was arrested; and 2 (4.3 per cent) are lost to follow-up.

If those patients who died of causes other than tuberculosis are considered as good surgical results, then 84 per cent of all patients followed up had successful results and 16 per cent were surgical failures. No detailed case histories are presented but representative roentgenograms of 2 patients are shown to illustrate the collapse obtained (Figs. 1 and 2).

Preoperative pulmonary function studies were performed on all but the earliest patients in this series. These studies were repeated between operation and about 2 months after the second operation. Several potential candidates for bilateral surgery were eliminated from surgical consideration because of inadequate respiratory reserve. In only one of the 46 patients in this series was the preoperative maximum breathing capacity less than 50 per cent of that predicted. The loss of ventilatory function varied greatly following each plombage procedure. The average loss of maximum breathing capacity was 8 L. per minute, but this figure varied from a loss of 30 L. to an actual gain of 6 L.

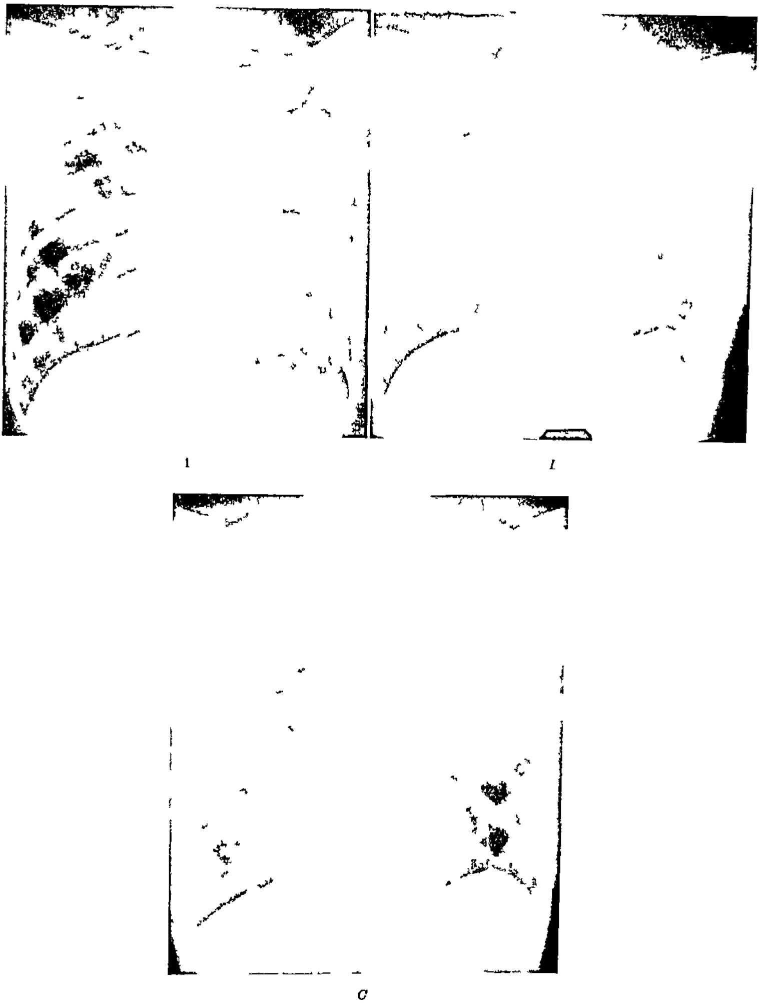
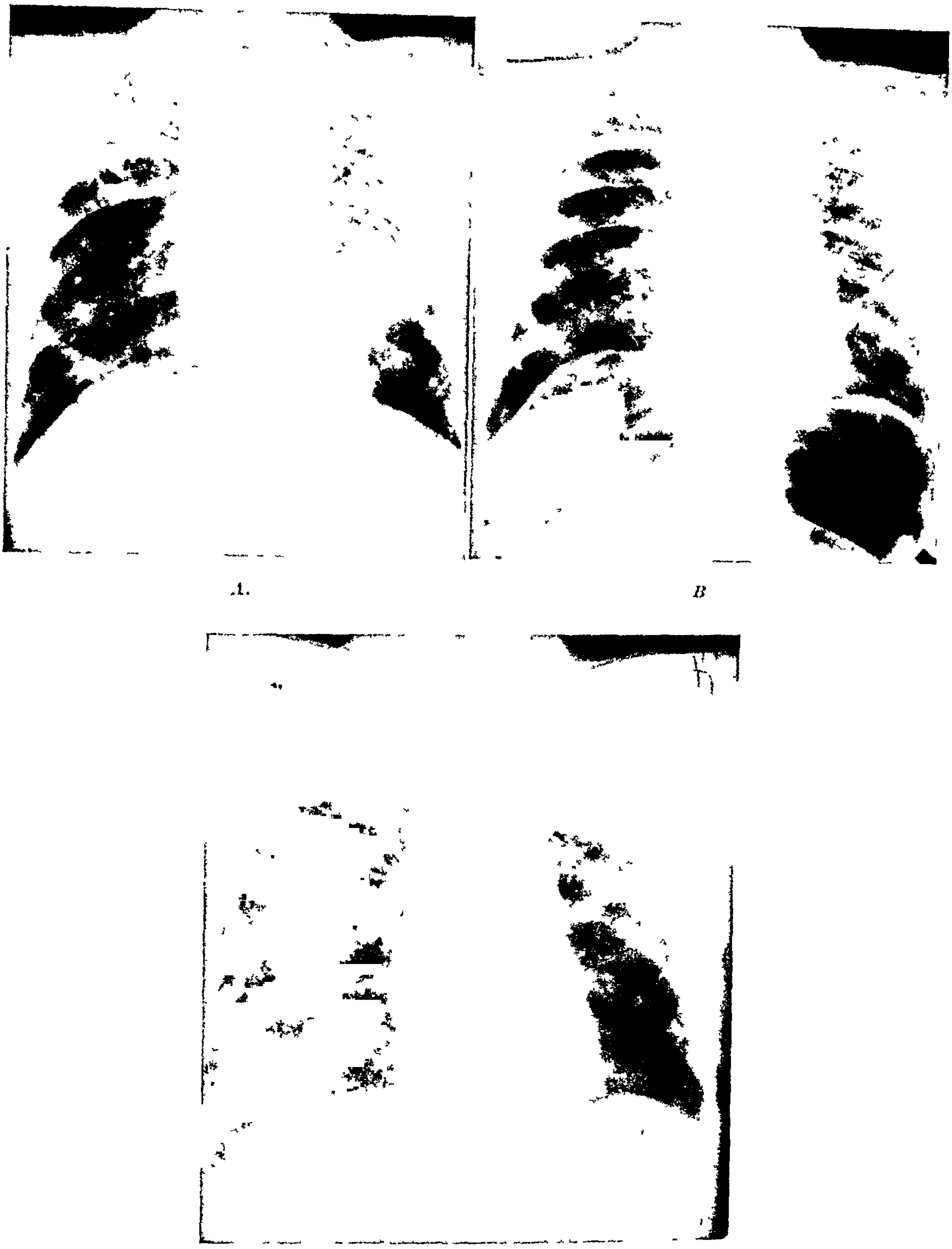


Fig 1.—*A* B. W., a 41 year old Negro man with positive sputum. Admission film of April 30, 1953.

B Preoperative film of June 10, 1954, following 14 months of chemotherapy and 3 months of pneumoperitoneum. Bilateral cavity persists and the sputum was persistently positive.

C Follow up film of Aug. 4, 1955, 4 months after discharge as inactive. The patient is well and working full time at present. Left plombage done on June 10, 1954, right Oct. 7, 1954.



A.

B

C.

Fig. 2.—*A*, A 54-year-old white male alcoholic with positive sputum. Admission film of Oct 14, 1953.

B, Preoperative film of March 29, 1955, following 15 months of chemotherapy and 12 months of pneumoperitoneum Sputum negative.

C, Follow-up film of Oct. 11, 1957, 15 months after discharge as "inactive." Patient is well and working full time at present Left plombage done on March 30, 1955; right, July 25, 1955.

per minute No patient became a "respiratory cripple" as a result of the bilateral collapse but, as noted above, one patient died 18 months postoperatively of progressive cor pulmonale and another with inactive disease is in chronic right heart failure 5 years after surgery The majority of the patients have no dyspnea even on considerable exertion

DISCUSSION

In the swing to resection in recent years some centers have abandoned all other forms of surgery but resection Thus a patient thought unfit for pulmonary resection is relegated to the group of unsalvageable "chronics" It seems paradoxical that now we try to fit all patients into the mold of resectional surgery rather than to tailor our surgical procedures to fit the patient's needs

We feel that the results obtained in this group of patients, who can truly be called "salvage" cases, are highly satisfactory Certainly many of the patients would still be in the sanitarium as a burden to the community rather than occupying the useful place in society that they now fill

SUMMARY

1 A series of 46 patients who have undergone bilateral thoracoplasty with *paraffin plombage* is presented

2 The indications for collapse versus resection are discussed

3 Mortality was zero, and no major complications were encountered

4 Of all patients followed, 84 per cent had successful results and 16 per cent were surgical failures

5 Thirty two (70 per cent) of the entire group of these "salvage" patients are now well and working full time, with a minimum follow up of one year, and in a majority a follow up of 2 years or more

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THE PRESENT STATUS OF PULMONARY RESECTION IN THE TREATMENT OF TUBERCULOSIS

Josiah Fuller, M.D., Duluth, Minn.*

RECENT medical literature[1-6] contains many reviews in support of the thesis that pulmonary resection combined with appropriate antibiotic therapy is a safe and effective method of treating pulmonary tuberculosis. Nevertheless, most sanatoriums in this area are experiencing a noticeable decline in the number of resections done. In an effort to consider some of the reasons for this, a review was made of 134 patients who had pulmonary resection in the treatment of their tuberculosis. This represents all of the patients for whom the author performed a pulmonary resection for tuberculosis from January, 1953, to June, 1956. These operations were done at Nopeming Sanatorium, Nopeming, Minnesota, and Middle River Sanatorium, Hawthorne, Wisconsin.

The average age of these patients was 37 and the ages ranged from 8 to 60 years. Forty-four per cent of the patients were over 40 years old. Seventy-five of the 134 patients were males. Fourteen per cent of the cases were classified as minimal tuberculosis, 44 per cent moderately advanced, and 42 per cent far advanced.

Thirty-five per cent of the patients were known to have had their tuberculosis for less than one year and 35 per cent of them had had their tuberculosis for over 5 years. One patient had had active tuberculosis for 33 years. Forty per cent of the patients had relapsed after one or more previous unsuccessful attempts at treating their tuberculosis. All of these patients received what might be called the modern antibiotic treatment, consisting of a combination of drugs, which in most cases included para-aminosalicylic acid with streptomycin or isoniazid. Seventy-five per cent of the patients received antibiotic therapy for 4 to 12 months preoperatively, and 65 per cent for 4 to 12 months postoperatively.

An effort was made to determine the indications for resection in each case by reviewing the sanatorium charts. In an individual patient, a decision for pulmonary resection is influenced by many subtle factors, such as the risk of surgery, his social habits, and how well it is thought he will take care of himself and cooperate with the follow-up efforts. However, the anatomic indications for resection in each case are listed in Table I. One hundred and forty-one

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*Department of Thoracic Surgery, The Duluth Clinic, Duluth, Minn.

resections were performed on these 134 patients. In 77 per cent of the cases, immediately before resection, sputum and gastric aspirations were negative for tuberculosis on culture or guinea pig inoculation. The indications for resection in these patients were residual nodular disease in 71 cases, x-ray evidence of cavity in 26 cases, and bronchial disease, which was usually bronchiectasis, in 7 cases, and in one case the resection was done to rule out malignancy. Sixteen per cent of the resections were done for a cavity with positive sputum and 8 per cent were done for persistently positive sputum without x-ray evidence of cavity.

TABLE I
INDICATIONS FOR RESECTION IN PULMONARY TUBERCULOSIS

	141 RESECTIONS	
	NUMBER	PERCENTAGE
Nodular residual disease	71	53
Cavity negative	26	18
Cavity positive	25	16
Positive without cavity	11	8
Bronchial disease	7	5
Rule out malignancy	1	<1

In 52 per cent of these 141 operations, a segmental resection was done, and in 19 per cent only a subsegment was removed. A lobectomy was done in 24 per cent of the cases and in only 7 patients was a pneumonectomy necessary. Five patients had bilateral resections performed. In 38 patients, all gross disease was removed as determined by palpation on the operated side, and by x-ray studies on the unoperated side.

The resected specimens were all dissected immediately, either by the pathologist or by the surgeon, and cultures taken from appropriate areas in all but one specimen. The lesions the pathologist felt were most significant in each specimen are classified in Table II. Any specimen in which there was demonstrated bronchial communication with a circumscribed mass of caseous material, and in which the bronchus was obstructed by the inspissated caseous material, was classified as a "filled cavity." This explains the 50 per cent incidence of cavity in this series. Actually, many of these were called "nodular residual" in x-ray interpretations. The 47 caseous nodules were parenchymal nodules without bronchial communication. The 18 cases called bronchial disease were either bronchiectasis or bronchostenosis. The four specimens in which fibrosis only was found could well be called healed tuberculosis, since tubercle bacilli were not demonstrated in any of them.

TABLE II
PATHOLOGY OF RESECTED SPECIMENS IN PULMONARY TUBERCULOSIS

	141 SPECIMENS	
	NUMBER	PERCENTAGE
Cavity	71	50
Caseous nodules	47	33
Bronchial disease	18	13
Fibrosis	4	3
Tuberculous pneumonitis	1	1

More important than the anatomic description of the resected specimen are the results of bacteriologic examinations In 45 per cent of the 140 specimens so studied, acid fast bacilli were demonstrated by stain only In an additional 39 per cent, the bacteria grew on culture or guinea pig inoculation This leaves 23 patients whose specimens did not demonstrate acid fast bacilli by our methods It is interesting that 7 of these patients had had positive pulmonary secretions immediately before surgery, and 6 of the 7 have been negative since their resection One wonders if more of these specimens might have been positive bacteriologically if rather than taking selective areas for culture, we ground up the entire specimen and studied the sediment

These patients were followed by x-ray studies and by bacteriologic testing, including sputum and gastric cultures, until it was felt sufficient stability had been demonstrated In many cases, this period of observation extended over 2 years After this, the patients were followed by repeated x-ray observation Thirty six per cent of them were followed for over 3 years and 67 per cent for over 2 years Only 6 per cent of the patients were followed for less than one year

The results of pulmonary resection in these cases are depicted in Table III The early mortality was in an obese 54 year old Indian woman with far-advanced bilateral tuberculosis A desperate attempt was made to resect a cavity during one of her repeated episodes of hemoptysis Although it appeared as though the immediate results were successful, she died 5 days postoperatively of a massive pulmonary embolus

TABLE III
RESULTS OF RESECTION THERAPY FOR PULMONARY TUBERCULOSIS

	134 CASES	
	NUMBER	PERCENTAGE
Inactive	123	92
Early mortality	1	1
Failure	10	7
Late mortality	6	4
Morbidity	13	10

The late deaths were all unrelated to tuberculosis and occurred 2 months to over 3 years after dismissal from the sanatorium They include such causes as auto accident, diabetic acidosis, alcoholism, pneumonia, coronary insufficiency, and carcinoma of the kidney All of these patients were inactive at the time of death and are so classified in Table III

Thirteen patients, or 10 per cent, had a significant amount of morbidity associated with their surgery In 12 instances, this was due to persistent air leak or pneumothorax space problems These all responded to appropriate corrective surgery

One hundred and twenty three patients, or 92 per cent, have been inactive since their resection and an additional 6 patients are inactive after subsequent treatment, which leaves only 4 treatment failures This method of treatment, then, eventually converted 97 per cent of these 134 patients to the inactive status

DISCUSSION

In spite of these satisfactory results, there were only 6 pulmonary resections for tuberculosis done in these two institutions in 1957. A study of the reasons for this change will lend some light on the present status of resection therapy in the treatment of pulmonary tuberculosis. The average sanatorium population in these two institutions has dropped from 226 in 1954 to 183 in 1957. Also, this population has become older and therefore a poorer risk for pulmonary resection. In November, 1954, 35 per cent of the patients were over 60 years old, while in November, 1957, 61 per cent were over 60.

When the resection program began in these institutions, there was a backlog of patients with chronic pulmonary tuberculosis from the pre-antibiotic era, who had been unsuccessfully treated by other methods such as bed rest, pneumothorax, pneumoperitoneum, or thoracoplasty. Today, the proper use of antibiotics, particularly isoniazid, is clearing the acute cases so that many patients are no longer left with a residual process to be resected. As experience accumulates with these drugs, phthisiologists are becoming more confident in their ability to prevent a relapse from residual areas of disease.

Today, the indications for pulmonary resection, after a period of antibiotic therapy, might be stated as follows: (1) persistently positive pulmonary secretions in the presence of localized disease; (2) x-ray evidence of an open cavity whether or not the pulmonary secretions have become negative on antibiotic therapy; (3) whenever there is doubt about the diagnosis of a pulmonary mass; and (4) significant residual nodular disease. Today this area of nodular disease must be larger, certainly greater than 2 cm. and more solid than it was a few years ago, to be considered an indication for pulmonary resection. If the nodule has appeared in a spot where there has been a previous cavity, a resection is more apt to be considered necessary to prevent a recurrence of active disease. A resection done in the presence of negative pulmonary secretions certainly must be considered prophylactic surgery and the time may come when the effectiveness of antibiotic therapy is such that the prophylactic resections mentioned above are no longer necessary.

SUMMARY

One hundred and thirty-four patients are presented who had pulmonary resection in the treatment of tuberculosis from January, 1953, to June, 1956. The surgical mortality rate was less than 1 per cent. The morbidity rate was 10 per cent, and 97 per cent of the patients were eventually converted to an inactive status. Only six pulmonary resections for tuberculosis were done in the same two institutions in 1957. The reasons for the marked decrease in surgery are decreasing number and increasing age of patients with tuberculosis in this area, and the effectiveness of the antituberculosis drugs in the treatment of new cases of tuberculosis.

After appropriate antibiotic therapy, present indications for pulmonary resection in the treatment of tuberculosis are as follows: (1) localized disease with persistently positive pulmonary secretions, (2) open cavity, (3) significant residual nodular disease, and (4) undiagnosed pulmonary mass

I wish to thank Dr R W Backus, Superintendent and Medical Director of Nopeming Sanatorium, and Dr S T Sundell, Former Superintendent and Medical Director of Middle River Sanatorium, for their assistance in obtaining information on these patients

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DISCUSSION

In spite of these satisfactory results, there were only 6 pulmonary resections for tuberculosis done in these two institutions in 1957. A study of the reasons for this change will lend some light on the present status of resection therapy in the treatment of pulmonary tuberculosis. The average sanatorium population in these two institutions has dropped from 226 in 1954 to 183 in 1957. Also, this population has become older and therefore a poorer risk for pulmonary resection. In November, 1954, 35 per cent of the patients were over 60 years old, while in November, 1957, 61 per cent were over 60.

When the resection program began in these institutions, there was a backlog of patients with chronic pulmonary tuberculosis from the pre-antibiotic era, who had been unsuccessfully treated by other methods such as bed rest, pneumothorax, pneumoperitoneum, or thoracoplasty. Today, the proper use of antibiotics. particularly isoniazid, is clearing the acute cases so that many patients are no longer left with a residual process to be resected. As experience accumulates with these drugs, phthisiologists are becoming more confident in their ability to prevent a relapse from residual areas of disease.

Today, the indications for pulmonary resection, after a period of antibiotic therapy, might be stated as follows: (1) persistently positive pulmonary secretions in the presence of localized disease; (2) x-ray evidence of an open cavity whether or not the pulmonary secretions have become negative on antibiotic therapy; (3) whenever there is doubt about the diagnosis of a pulmonary mass; and (4) significant residual nodular disease. Today this area of nodular disease must be larger, certainly greater than 2 cm. and more solid than it was a few years ago, to be considered an indication for pulmonary resection. If the nodule has appeared in a spot where there has been a previous cavity, a resection is more apt to be considered necessary to prevent a recurrence of active disease. A resection done in the presence of negative pulmonary secretions certainly must be considered prophylactic surgery and the time may come when the effectiveness of antibiotic therapy is such that the prophylactic resections mentioned above are no longer necessary.

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SEGMENTAL PULMONARY RESECTION WITH INITIAL PERIPHERAL DISSECTION

John D. Steele, M.D., San Fernando, Calif.

Most authors,[1-6] in describing the technique of segmental pulmonary resection, advocate starting the dissection by isolating the segmental bronchus and artery; they then develop the interlobar plane as the dissection proceeds peripherally, ligating the branches of the interlobar vein as encountered.

Only Chamberlain and Ryan[5] mention the possibility of using occasionally an "outside-in" technique for cysts, atelectatic segments, and chronic lung abscesses.

Several years ago, we started performing subsegmental resections for isolated pulmonary nodules using an anatomic dissection rather than the clamp ("wedge") technique. The ease with which anatomic subsegmental planes could be developed so impressed us that we decided to extend this type of resection to entire segments.

We now use initial peripheral dissection in the great majority of our segmental resections, and believe it has the following advantages:

1. When a segment is distorted by disease, hilar dissection may be confusing and there is danger of compromising the bronchial and arterial supply to neighboring undiseased segments. When dissection is started at the periphery, only the portion of the lung containing the disease is resected accurately. Often it may not be apparent until the completion of the dissection as to just what anatomic division of the lobe has been resected. In some instances, the disease will involve only a large subsegment whereas in others it will be found that an entire segment, together with an involved adjacent subsegment of a distended neighboring segment, has been resected. In either case, the correct amount of lung, and no more, will have been resected.

2. Recent precise anatomic studies have demonstrated that there may be considerable crossing of intersegmental lines by arteries, veins, and segmental bronchi and that anatomic hazards must be clearly understood if accurate segmental resections are to be performed.[7] Such variations in arterial and bronchial patterns may be difficult to recognize in initial hilar dissection, but are usually easily recognized when the intersegmental plane is developed from the periphery.

3. When using peripheral dissection, it is possible to leave stumps of the arterial branches approximately 1 cm. in length, and it is usually not necessary

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From the Veterans Administration Hospital, San Fernando, Calif., and from the Department of Surgery, University of California, Los Angeles, Calif.

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to expose the main stem artery. The stumps so remaining can be clamped safely if bleeding should occur. In hilar dissection, a tear of a segmental artery at, or close to, the main stem artery can be dangerous and difficult to control. The longer stumps are also an advantage when lymph nodes are adherent to the hilar structures.

4. Because of the above advantages of peripheral dissection, we feel that a safe, accurate segmental resection can be performed by a surgeon who has had less experience with the operation than is the case when hilar dissection is employed.

TECHNIQUE

After interpleural adhesions have been divided, and it has been decided that a segmental resection is to be performed, dissection is started by making an incision through the visceral pleura into an interlobular plane with the lung well inflated (Fig. 1, *a*). It is usually advisable to leave one lobule between the area of disease and the line of incision. The lobules are, of course, characteristically outlined by carbon pigment deposited in the interlobular lymphatics.

Often, by the repeated application of varying degrees of positive pressure through the intratracheal tube, the location of the intersegmental plane will become apparent due to a lag in the filling of the periphery of the involved segment. It is advisable to mark the line of demarcation by a series of small interlobular incisions with the scissors so that dissection can be attempted in these areas even after the lung is completely inflated and the demarcation line is no longer apparent.

After the initial incision has been made, further limited dissection is carried out by blunt dissection using scissors (Fig. 1, *b*). If a well-developed, undiseased intersegmental plane has been entered, dissection will proceed with ease. If the proper plane has not been entered or, if the disease extends across the intersegmental plane, dissection should be abandoned at this point and attempted in another area.

When blunt instrument dissection has proceeded satisfactorily for a few centimeters, further dissection is carried out with the finger (Fig. 1, *c*). The sense of touch will aid in determining whether the intersegmental plane has been entered. If so, dissection will proceed with very little resistance. If there is appreciable resistance, dissection should be started again at another point as noted above.

Of course, the only intersegmental structures which are normally encountered during such peripheral dissection are branches of the intersegmental vein (Fig. 1, *b*) These are ligated on both sides and divided. As the dissection proceeds, the intersegmental vein usually is visualized and can be preserved, leaving it attached to the adjacent segment.

As dissection proceeds toward the hilum of the segment, the branches of the segmental arteries and bronchi come into view. These branches can be followed to within approximately 1 cm. of the hilum of the segment, and divided between ligatures at this point (Fig. 1, *d*).

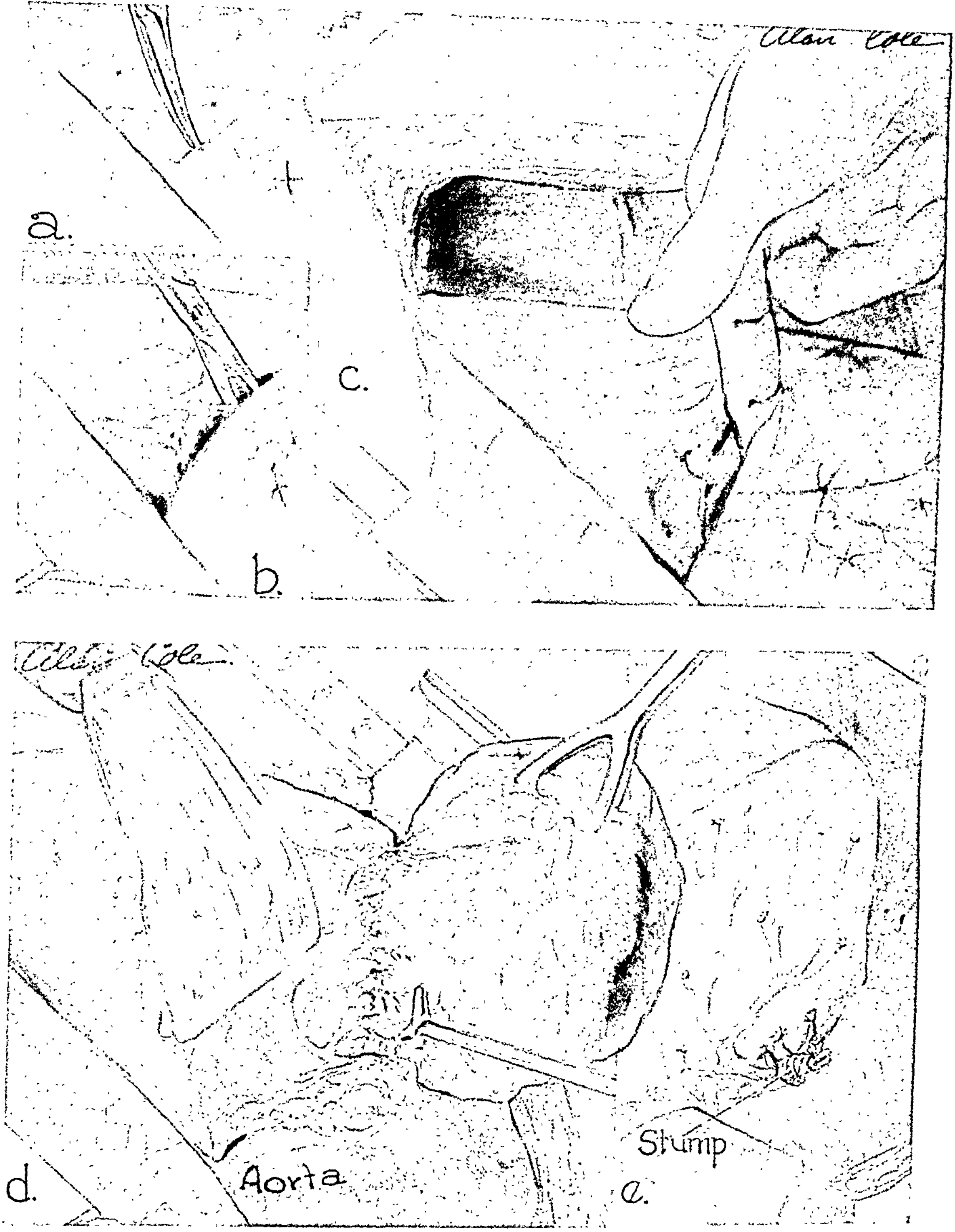

Fig. 1.—*a*, Start of resection of apical-posterior segment of left lung. Incision is made with the scissors through the visceral pleura into an interlobular plane.

b, Further dissection is carried out by blunt dissection with scissors. Branches of the intersegmental vein can be seen crossing the intersegmental plane.

c, Final identification and further dissection in intersegmental plane using finger.

d, Dissection of branches of segmental bronchus and artery close to hilum of the apical-posterior segment on left. The instrument has been passed under a branch of the artery.

e, The stumps of the branches of the segmental bronchus and segmental arteries which have been ligated approximately 1 cm. distal to the surface of the pulmonary artery. Branches of the intersegmental vein are seen on the intersegmental surface of the adjacent anterior segment.

It is not necessary to dissect through the entire intersegmental plane before starting to divide the arteries and bronchi. Actually, subsequent dissection will be facilitated if only a portion of the intersegmental plane is developed first—enough to allow division of at least one main branch of the segmental artery and bronchus. Dissection of a small, final portion of the intersegmental plane can be postponed until all branches of the artery and bronchus have been divided.

The stump containing the ligated branches of the segmental artery (or arteries) and the bronchial stumps, is shown in Fig. 1, *e*.

Sometimes, after full inflation of the remaining lung, a lobule or two on the raw surface of the adjacent segment will appear to be unaerated, or to hang free. It is advisable to resect such lobules, after ligating the pedicle.

We have performed at least 200 segmental resections using this technique; in fact, we use it for the great majority of our segmental resections. Occasionally, when the peripheral portion of the intersegmental plane cannot be identified accurately, we resort to initial hilar dissection. This has occurred more frequently with the superior segments of the lower lobes than with any other segments.

SUMMARY

A method of dissection is described for segmental pulmonary resection, starting at the periphery of the segment, ligating vessels and bronchi as they are encountered. This method is more accurate than initial hilar dissection in segments distorted by disease, and where there are anomalies in arterial and bronchial patterns. Operative accidents are less likely to occur with peripheral dissection than when initial hilar dissection is employed. Over 200 segmental pulmonary resections have been performed satisfactorily with initial peripheral dissection.

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BRONCHOTRACHEAL ANASTOMOSIS

A Follow-Up of 9 Cases on the Left Side and 7 on the Right

Viking Olov Björk, M.D., Uppsala, Sweden*

In cases of pulmonary tuberculosis with main bronchus stenosis every effort is made to avoid a total pneumonectomy. If a part of the lung is healthy with a normal bronchus, this bronchus can be anastomosed end-to-side to the trachea after resection of the diseased portion of the lung, together with the stenosed main bronchus. The remaining part of the lung can then function normally, and there is very little risk that stricture will occur at the anastomosis. Direct anastomosis has been preferred to the skin grafting procedure devised by Gebauer. The danger of suturing a skin graft, reinforced with stainless steel or silver wire, into the side of a main bronchus, narrowed by an old tuberculous infection, is obvious. The metal thread may erode through the skin, necessitating its removal followed by secondary stricture and bronchiectasis. These objections make direct anastomosis preferable. The object of this paper is to give our experiences in 16 cases followed 1 to 5 years.

MATERIAL

Eleven women and 4 men underwent bronchotracheal anastomosis for pulmonary tuberculosis (Tables I and II). The oldest patient was 58 years old, the youngest 20. A 48-year-old man underwent bronchotracheal anastomosis after resection for cancer.

INDICATIONS

In 10 cases, the diameter of the stenosed main bronchus was only 3 to 4 mm. and in the remaining cases slightly more. The widest stricture resected was 5 to 6 mm. Only the left main bronchus was left in this instance, the upper lobe with its completely stenosed bronchus having been removed at another hospital. A year later it was necessary to resect the main bronchus and perform an anastomosis which would have been technically much easier at the first operation, together with the lobectomy. I, therefore, consider that the main bronchus should be resected if it is narrowed down to 6 mm. in diameter. Complications may be expected if the resection is carried out peripheral to a main bronchus stenosis.

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*Chief: Thoracic Surgical Service, University Clinic, Uppsala, Sweden.

TABLE I RESULT OF PULMONARY RESECTION WITH BRONCHOTRACHEAL ANASTOMOSIS FOR PULMONARY TUBERCULOSIS ON THE RIGHT SIDE

CASE	OPERATION PERFORMED	OBSERVATION (YEARS)	CONDITION OF ANASTOMOSIS	FUNCTION OF RIGHT LUNG IN PER CENT OF TOTAL FUNCTION		
				OXYGEN UPTAKE	VENTILATION	VITAL CAPACITY
1 33 year old woman	Resection of right upper lobe + right main bronchus + anastomosis of right intermediate bronchus to trachea + extrapleural plombage	5	Good, open for 9 mm			
2 52 year old woman	Resection of right upper lobe + wedge right lower lobe + decortication + anastomosis of intermediate bronchus to trachea + osteoplastic thoracoplasty	1	Good, open for 7 mm			
3 40 year old woman	Resection right upper lobe + anastomosis of intermediate bronchus to trachea + extirpation of pericardial cyst	2	Good wide open	39	43	45
4 42 year old man	I Resection right upper lobe + anastomosis of intermediate bronchus to trachea	3 mo	Stenosis			
	II Resection of site of anastomosis with new bronchotracheal anastomosis 3 months later	1	Good, wide open	30	43	40
5 38 year old woman	Resection right upper lobe + superior segment right lower lobe + anastomosis of intermediate bronchus to trachea	2	Good, wide open	40	43	45
6 32 year old woman	Resection of right lower and middle lobes + main bronchus + anastomosis of right upper lobe bronchus to trachea under an old 11 rib thoracoplasty performed in 3 stages 5 years earlier, see Figs 1, *1 C*	4	Good, wide open	15	17	15
7 54 year old woman	Resection right lower and middle lobes + main bronchus + anastomosis of right upper lobe bronchus to trachea	2	Good, wide open			

TECHNIQUE

The operation can be performed in the lateral position, but I prefer to have the patient face down A Carlens' tube will considerably facilitate operations on the right side On the left side the anastomosis is usually performed on the open bronchus with intermittent occlusion or with the aid of Green's tube Occasionally a super Satinsky clamp has been applied to the side of the trachea A wide mobilization of the trachea, the bronchus, and the artery and vein of the remaining lung is advisable in order to perform the anastomosis with as little tension as possible The pulmonary ligament should be divided

TABLE II. RESULT OF LEFT-SIDED BRONCHOTRACHEAL ANASTOMOSIS

CASE	OPERATION PERFORMED	OBSERVATION (YEARS)	CONDITION OF ANASTOMOSIS
8. 32-year-old woman	Resection left upper lobe + main bronchus + anastomosis of left lower lobe bronchus to trachea after mobilization of the aorta + osteoplastic thoracoplasty	4	Good; open for 7 mm. in diameter
9. 30-year-old man	Resection left upper lobe + main bronchus + anastomosis of left lower lobe to trachea after mobilization of aorta	1½	Stenosis; atelectasis of lung behind stenosis; died from hemoptysis
10. 20-year-old man	Resection left upper lobe + main broncheus + anastomosis of left lower lobe to trachea	1½	Good, wide open; basal segments normal; bronchiectasis of superior segment
11. 43-year-old man	Resection left upper lobe + main bronchus + anastomosis of left lower lobe to main bronchus, 1 cm. below the carina	1½	Good; wide open
12. 30-year-old man	Resection left main bronchus + anastomosis of lower lobe to trachea. After mobilization of the aorta, there was a very pronounced tension on the suture line; left upper lobe had been removed one year earlier	2	Good; wide open
13. 25-year-old woman	Resection left upper lobe + main bronchus + anastomosis of left lower lobe to main bronchus, 2 cm. below carina	3	Good; wide open
14. 38-year-old woman	Resection left upper lobe + left main bronchus + anastomosis of left lower lobe bronchus to trachea after mobilization of the aorta	3	Good; wide open anastomosis; bronchography shows narrowing of superior segmental bronchus; basal segments normal
15. 28-year-old man	Resection left upper lobe + superior segment left lower lobe + main bronchus + anastomosis of basal segmental bronchus to main bronchus, 2 cm. below carina + osteoplastic thoracoplasty	3	Stenosis, open for 4 to 5 mm.; good aeration of lung behind stenosis
16. 48-year-old man	Resection right lung + 3 cm. lower trachea + 2 cm. left main bronchus + anastomosis of left main bronchus to trachea, end-to-end	1	Stricture; died (See Figs. 2 and 3)

Fine (3-0) chromic catgut on atraumatic needles as suture material is essential for a successful result. When silk was used in the beginning, it was necessary to remove the sutures by bronchoscopy as they caused suture granulomas which obstructed the lumen.

It is not necessary to cover the anastomosis by a pleural flap. It is usually found to be airtight immediately and will be covered by lung and mediastinal tissue. A pedicled pleural flap around the anastomosis may cause stricture.

It is unnecessary to perform a tracheostomy immediately after surgery. Most patients are able to raise sputum effectively. Only in 2 patients has a tracheostomy been performed; in Case 4, in which prolonged anoxia during anesthesia caused unconsciousness for 15 hours, and in the patient with cancer, Case 16.

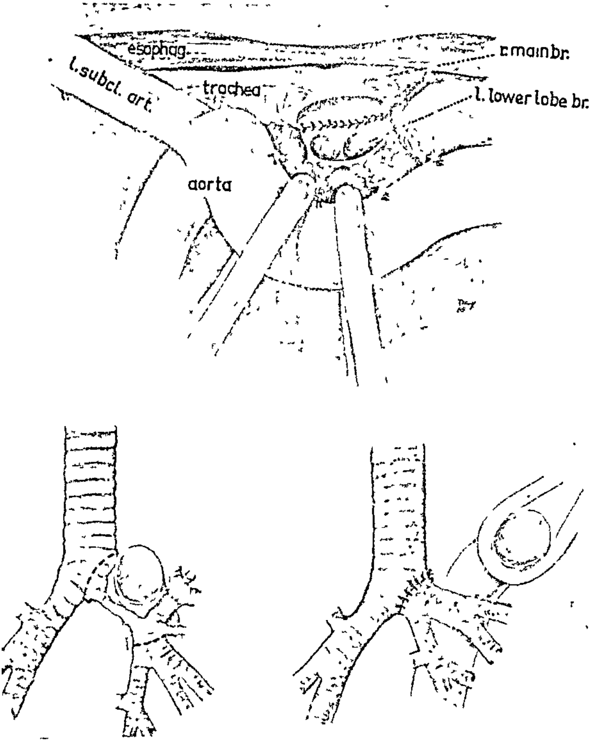

Fig. 1.—After division of the upper 4 to 5 pairs of intercostal arteries, the aorta is mobilized forward and the anastomosis performed behind the aorta. This was done in 4 cases. (From J. Thoracic Surg. 30: 194, 1955.)

Bronchoscopy has been performed routinely at intervals postoperatively. In cases in which catgut was used as suture material only an occasional granuloma has been removed.

Mobilization of the aorta was performed 4 times, greatly facilitating a left-sided bronchotracheal anastomosis (Fig. 1). In Case 10, an aortic mobilization was not done and the anastomosis to the trachea was very difficult.

During the traction on the aorta the recurrent nerve was damaged. In this case, mobilization of the aorta with a retroaortic anastomosis should have been done.

RESULTS

Mortality.—There was no immediate mortality. Two patients, Cases 9 and 16, died later, 1½ and 1 year after the operation. The main cause of death was stenosis at the site of anastomosis.

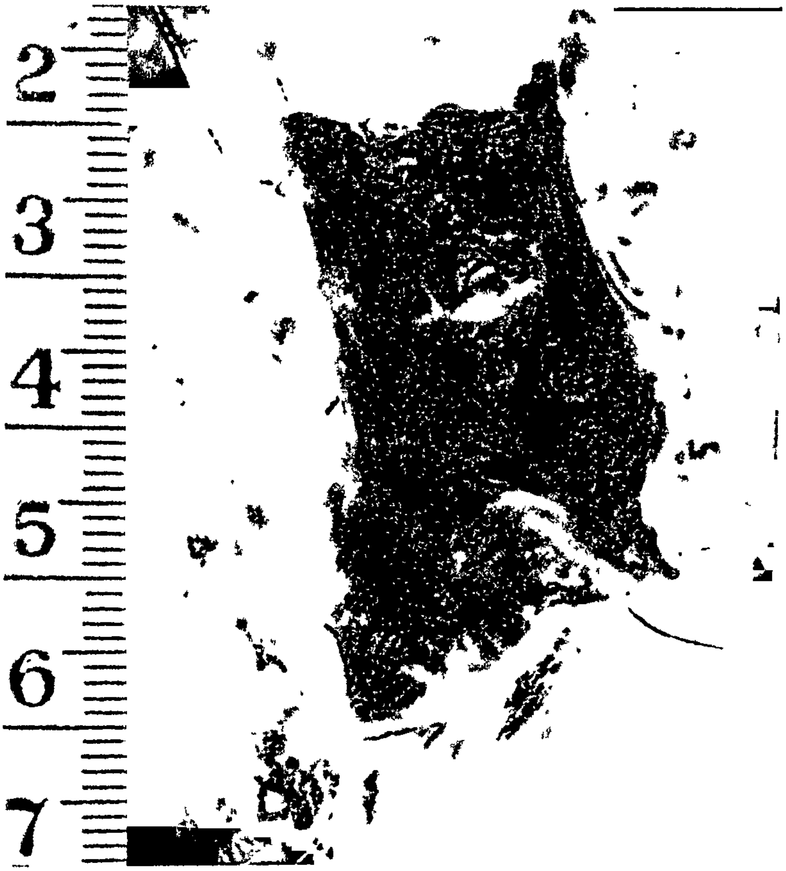

Fig. 2.—Case 16 Photograph demonstrating the specimen after removal, in one block, of the entire right lung with the lower part of trachea, the carina, and the first part of the left main bronchus.

Postoperative Complications.—No special immediate postoperative complication was encountered. Two patients of the 16 needed tracheostomy and in 2 other patients it was necessary to institute closed drainage for a second time; in one case due to air leakage, in the other due to an empyema. In spite of the surrounding infection, the anastomosis healed after prompt drainage of the infected space.

The most serious complication was a stricture at the site of the anastomosis. In 12 cases a good result with a wide open anastomosis was obtained. In these cases no bronchiectasis was found, and the function when studied was found excellent.

Stenosis was encountered in 4 cases

1. In Case 15, in which the basal segmental bronchus was anastomosed to the main left bronchus, 2 cm. below the carina, only a narrow lumen was present from the beginning. Three years later, there is only a 4 mm. lumen down to the basal segments. When the patient gets a cold there are sounds of stenosis on the left side. The patient is negative for the tubercle bacillus and is working full time.

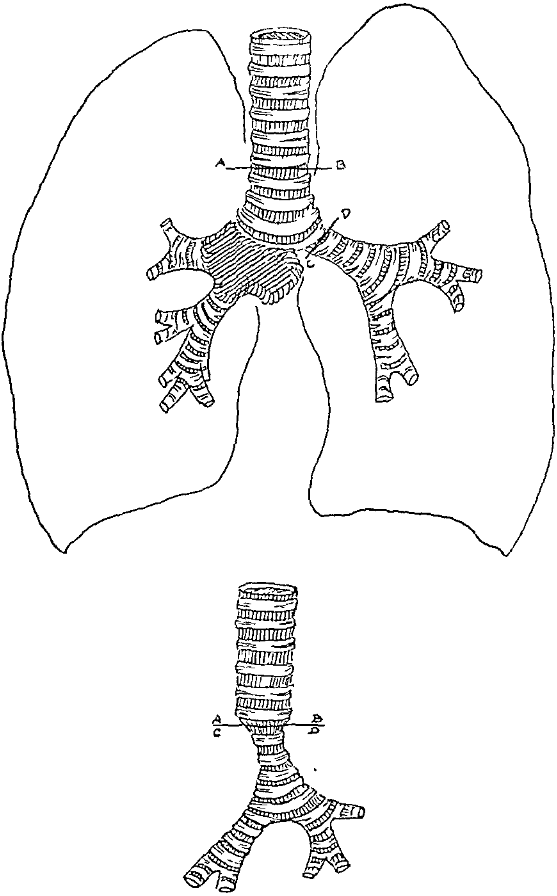

Fig 3.—Case 16. Diagram of the resection with end-to-end anastomosis of the left main bronchus to the trachea.

In Case 9, it was extremely difficult to complete the bronchotracheal anastomosis due to the bad quality of the wall of the lower lobe bronchus which was soft and friable. When the anastomosis was completed, the healthy parenchyma of the lower lobe ventilated well and was left in place. After 3 months, the lower lobe was completely atelectatic due to stricture at the anastomosis, although a suction tube could easily be passed down into the lobe. The patient refused re-operation although I tried to convince him that a pneumonectomy was necessary. After one year he was re-admitted for surgery with lower lobe atelectasis and extensive bronchiectasis. While receiving preoperative chemotherapy, he suddenly died from hemoptysis. The anastomosis was narrowed by tuberculous granulations and ulceration, and the lobe was destroyed by bronchiectasis.

3. In Case 4, resection of the right upper lobe plus the right main bronchus and a bronchotracheal anastomosis were performed. The quality of the bronchial wall was questionable. The anastomosis gradually became narrowed, probably due to an acute inflammatory reaction in the suture line. Three months after the first operation he was re-operated upon with the expectation of doing a pneumonectomy. A localized stricture at the anastomosis was found, and this stricture was excised. A new bronchotracheal anastomosis was performed, making the side hole in the trachea as big as possible. This anastomosis has remained wide open for one year.

4. In Case 16, too much tension occurred at the anastomosis between trachea and the left main bronchus after resection of the right lung including the carina and part of the left main bronchus and trachea (Figs. 2 and 3). The suture line gave way and a long stricture developed, resistant to dilatation. The patient died one year later from the stricture. Autopsy did not reveal any metastasis.

All patients were negative on culture for the tubercle bacillus except one (Case 8) in whom the guinea pig test was negative 3 years after resection and then turned positive. All living patients were back at work full time.

CONCLUSION

These experiences indicate that bronchotracheal anastomosis can be performed with an excellent result anastomically and functionally. There is, however, a great difference between handling the left- and the right-sided cases.

Left-Sided Cases.—A direct anastomosis between the left main bronchus and the trachea, as in Case 16, cannot be performed without considerable tension. The tracheobronchial tree is stretched over the aortic arch and too much tension may cause rupture of the anastomosis with stricture. Furthermore, the continuous hammering of the aortic pulsations on the overstretched tracheobronchial tree may cause degeneration and softening of the bronchial cartilages and stricture. In Case 9, in which the anastomosis became stenosed resulting in an atelectasis in a few months after operation, there was no disruption of the anastomotic line. At autopsy, the cause of stenosis was found to be progression of the tuberculous endobronchitis with ulceration and tuberculous granulations at the anastomosis.

From these experiences the following conclusions may be drawn concerning left-sided bronchotracheal anastomosis:

1. As there will always be some tension at the anastomosis, a bronchotracheal anastomosis should only be performed on a healthy bronchus with strong cartilages.

2. If an ideal local result is not obtained, one should not hesitate to do an immediate pneumonectomy in spite of all previous efforts to save lung tissue.

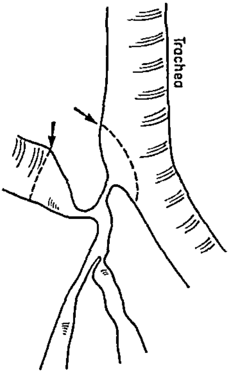

Fig 4.—*A*, Case 6. Diagram of the bronchial resection which saved the right upper lobe under an old 11-rib thoracoplasty resulting in 15 per cent oxygen uptake on that side.

3. If late atelectasis occurs after some months and there is no complete stricture at the anastomosis, it is due to degeneration of cartilages in the bronchial wall or to a tuberculous endobronchitis. As there is no possibility of doing a reresection with a new anastomosis in healthy bronchial wall, a total resection of the remaining lung should be done, once the condition is diagnosed.

Right-Sided Cases.—On the right side where no interference is presented by the aorta, the principle of handling these cases is completely different.

In Case 4, a stricture was found at the anastomosis which was due to a local inflammatory reaction. Therefore, at re-operation, the stenosed anastomosis could be resected and a new junction made to a large hole in the side of the trachea. Here it was important to make the tracheal hole large and to excise peripherally in healthy bronchial tissue. Due to the absence of the aorta, more tension is allowed on the suture line on the right side.

Fig. 1.—Cont'd. *B*, Case 6. X-ray film of this patient with a preserved right upper lobe, 4 years after the bronchotracheal anastomosis.

C, Case 6. Bronchography shows a wide open bronchotracheal anastomosis to the right upper lobe with a normal bronchial tree, 4 years after the anastomosis.

It is important to realize that a good result may be obtained by bronchotracheal anastomosis under an old 11 rib thoracoplasty as in Case 6, in whom, after anastomosis of the right upper lobe to the trachea, there remained an oxygen uptake of 15 per cent on the right side 4 years after the operation (Figs. 4, *A*—*C*).

SUMMARY

A review of the results in 16 bronchotracheal anastomoses shows that in 9 left-sided cases, stenosis occurred in 3 instances. In one of these the rupture of the anastomosis and the degeneration of cartilage was ascribed to the continuous hammering of the aorta on the tense and overstretched bronchotracheal segment. The secondary atelectasis should be treated by resection of the remaining lung.

On the right side, a bronchotracheal anastomosis in 7 cases resulted in only one stricture. This was considered due to an inflammatory reaction, as the anastomosis was made in diseased bronchial tissue. A re-resection in healthy tissue with a new bronchotracheal anastomosis gave an excellent result in spite of the pronounced tension on the suture line at the time of surgery.

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INTESTINAL DUPLICATION CYST OF ABDOMINAL ORIGIN PRESENTING IN THORAX

Report of a Case

Harold C. Spear, M.D., DeWitt C. Daughtry, M.D., and John G. Chesney, M.D., Miami, Fla.*

In 1950, Gross, Neuhauser, and Longino[1] reported their experiences with 3 unusual cases of intestinal diverticula which originated from duodenum or jejunum, extended through small hiatuses in the right crus of the diaphragm, and expanded within the thorax to present as large cystic masses. It is our purpose in this communication to report an additional example of an intestinal diverticulum which extended through the right diaphragm to present as a large cystic mass in the right hemithorax.

The symptoms produced by these diverticula, all of which were discovered during infancy, were related either to the compression effects of a large space-occupying lesion on the cardiorespiratory system or to the digestive action of the acid gastric juice secreted by the lining cells. In each of the 3 cases reported, the stalk of the diverticulum was a patent process which communicated with the duodenum or jejunum. Accordingly, in 2 of the 3 cases, chest x-ray study revealed the thoracic diverticulum to contain both air and fluid; in the third case no air was noted. Also, barium was observed to enter the diverticulum in one case. Treatment in each case consisted of excision of the diverticulum, employing both thoracic and abdominal approaches. Our case represents a variant from the 3 cases reported in that the stalk of the diverticulum was not patulous and we were able to accomplish total excision by a right thoracic approach alone.

CASE REPORT

R. B., a 3-week-old white male infant, was referred to us on Aug. 13, 1958, with the chief complaint of episodes of cough, dyspnea, and cyanosis of 3 or 4 days' duration. His parents observed that he had had a harsh cough essentially since birth, and that this had increased in frequency and severity. The cough was not always related to feedings; but he did not take his feedings normally and frequently regurgitated. During the past 3 to 4 days, the patient had developed paroxysmal episodes of cough and respiratory difficulty associated with cyanosis. A chest x-ray was taken on Aug. 12, 1958, which revealed a large rounded mass located in the posterior portion of the right hemithorax (Fig. 1). The patient was hospitalized for further diagnostic study. Family history was significant in that a sister had had a sacrococcygeal teratoma.

Physical examination revealed a fairly well-developed and well-nourished white male infant who was subject to paroxysms of coughing, occasionally associated with respiratory distress and cyanosis. Examination of the chest revealed symmetrical expansion without evidence of intercostal retraction. Although there was no respiratory stridor, there were both inspiratory and expiratory wheezes audible over both lung fields, but accentuated on the right side, which were suggestive of respiratory obstruction. The heart was normal and the remainder of the physical examination was unremarkable.

From the Department of Surgery, University of Miami School of Medicine, Miami, Fla.

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*Present address: 1550 N.W. 10th Ave., Miami, Fla.

Routine laboratory studies, including complete blood count, urinalysis, and an electrocardiogram, were within normal limits. Barium swallow under fluoroscopy* revealed the esophagus to be midline, not deviated or impinged upon by the large posterior thoracic mass. The mass itself occupied the lower two thirds of the right posterior hemithorax. It was not pulsatile. No barium entered the mass. Several anomalous vertebrae were noted both in the upper and mid thoracic spine.

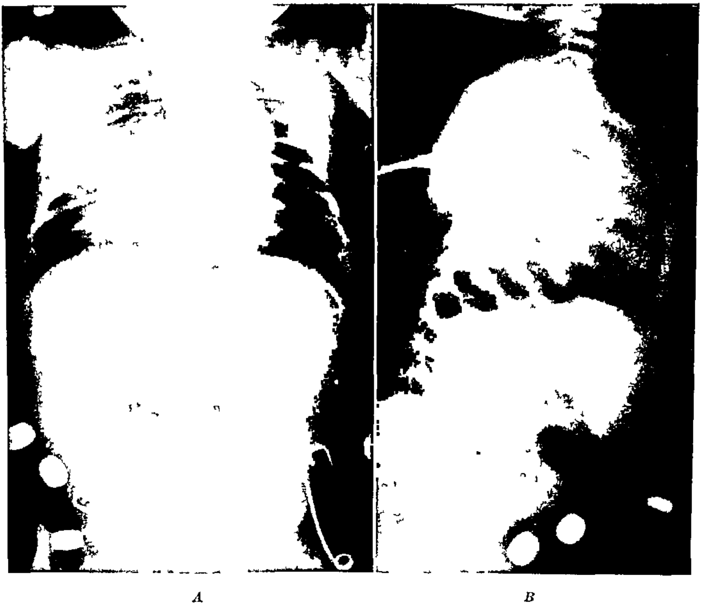

Fig. 1.—*A* and *B* illustrate large rounded mass located in the right posterior chest.

Because of the posterior location of the mass and the adjacent anomalous thoracic vertebrae, a pantopaque myelogram† was performed to exclude the possibility of an intrathoracic meningocele. This study failed to demonstrate any communication between the subdural space and the thoracic mass, nor was any defect noted within the spinal canal. In order to delineate the lesion a little more clearly, PA and lateral laminograms were made. These showed the mass to be discrete from the cardiac shadow.

Operation was undertaken on Aug. 15, 1958, under general anesthesia with endotracheal intubation. Right thoracotomy was performed through the fifth intercostal space. Upon opening the pleural space, an extremely tense, pear shaped cystic mass was encountered, firmly attached to the posterior thoracic wall and covered by parietal pleura. The mass had apparently compressed the right lower lobe from birth, as this lobe was totally atelectatic in the rubbery carnified manner of fetal atelectasis. The mass extended to the upper third of the right hemithorax and was firmly anchored to the posterior gutter and adjacent vertebral column. The pleura was incised about the upper margin of the mass and retrograde dissection was carried out. There were many small blood vessels entering the thoracic parietes. As the mass was dissected inferiorly toward the di

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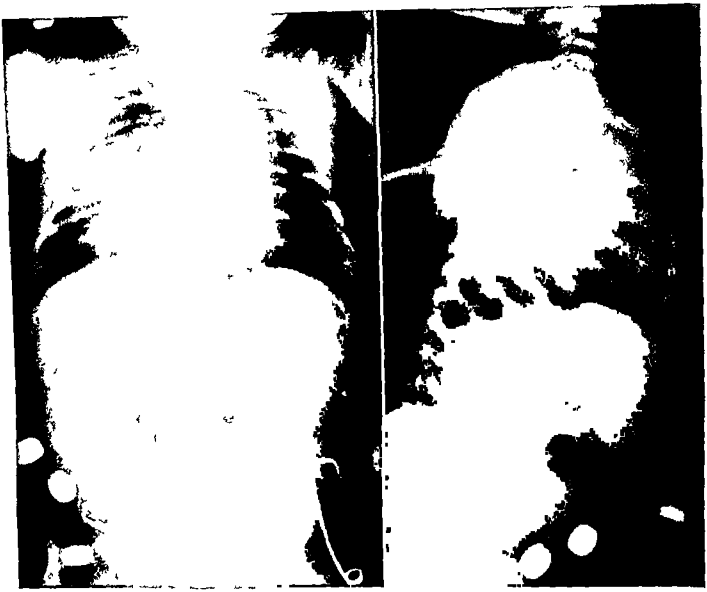

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*Performed by Dr Raymond E Parks

†Performed by Dr Robert S Tolmach.

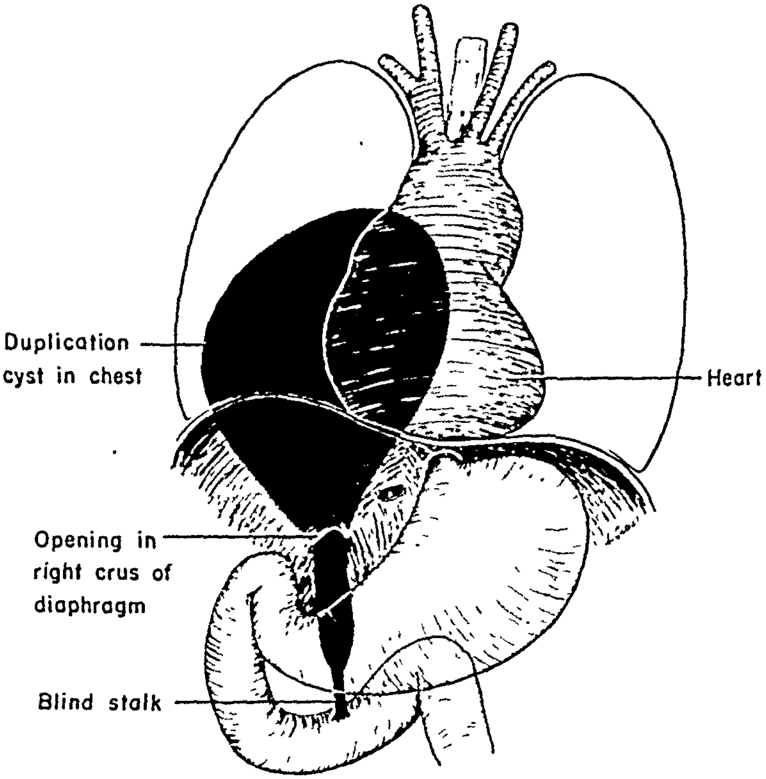

Fig. 2.—Diagrammatic representation of the cyst revealing its stalk-like extension through the right crus of the diaphragm and its origin from the duodenum in the vicinity of the superior mesenteric vessels.

The cyst was amputated through its stalk and the specimen was then injected with saline solution in order to confirm the presence of a blind proximal end. After the proximal end was indeed found to be watertight, attention was turned to the small hiatus through which the cyst had traversed the diaphragm. This hiatus was located to the right of the vertebral column, quite distinct from the esophageal hiatus, and had no posterior rim of tissue which could be used for repair. However, after removal of the cyst, the hiatus became so small that it did not seem necessary to carry out any type of plastic repair, particularly since it led only into the retroperitoneal space rather than into the peritoneum proper.

The previously totally atelectatic right lower lobe was then partially inflated by the continuous application of positive pressure insufflation. A small radiopaque catheter was brought out through a stab wound inferiorly in the midaxillary line and was connected to a subaqueous drainage system, after which chest closure was carried out.

Postoperatively, the infant made an entirely uneventful recovery. Chest films on Aug. 20, 1958, revealed the right lung to be completely expanded. He was discharged home on the tenth postoperative day, entirely free of symptoms.

Study of the excised specimen revealed an intestinal cyst consisting of an outer layer of longitudinal and an inner layer of circular muscle, with a well-defined submucosa and muscularis mucosa. The mucosal lining contained both gastric and intestinal secretory elements (Fig. 3).

DISCUSSION

Our case conforms to the 3 cases previously reported in which a cystlike diverticulum arose from the small intestine by a slender stalk and traversed the right diaphragm through a small hiatus to present as a large cystic mass in the thorax. In our case, there was no free communication between the diverticulum and the intestine from which it arose because the proximal end of the stalk was not patent. Our patient (age 3 weeks) was considerably younger than those previously reported (ages 3½ months, 4 months, and 4 years) and was operated upon as semi-emergency, once the diagnostic studies had been completed, in view of the progressive nature of the paroxysms of cough, respiratory distress, and cyanosis. We surmise that the progressive nature of the symptomatology related to the secretion of gastric and intestinal juices under mounting tension with resultant expansion of the cyst wall and increasing compression effects. A specimen of the contained secretion was found to exhibit no tryptic activity, but, through an error, was not tested for acidity. However, the cyst wall showed no evidence of the ulceration or intense inflammation which one might anticipate if acid and pepsin were present.

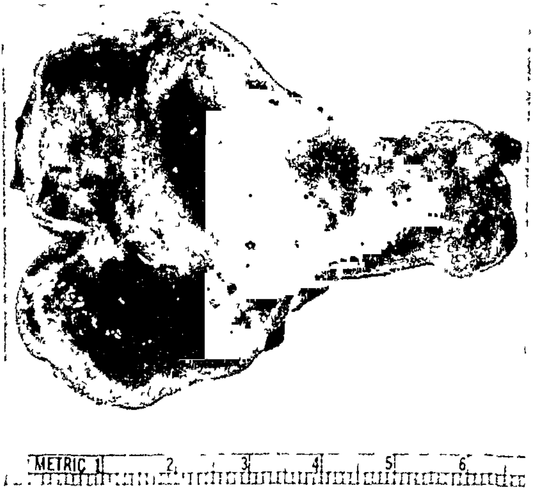

Fig 3.—The cyst has been opened longitudinally to reveal the glistening mucosal lining and the rugal pattern at the proximal (smaller) end. A small projection of the retracted blind stalk can also be visualized.

Radiologically, there appeared to be a solid space occupying mass in the right posterior thorax. A differential diagnosis of neuroblastoma or some other variety of neurogenic tumor, internal meningocele, bronchogenic or esophageal duplication cyst, teratoma, and intrapulmonary h[illegible] [illegible] sider

In view of the configuration of the mass and the absence of contained air, the diagnosis of diaphragmatic hernia of Bochdalek foramen variety was not seriously considered and did not confound the problem as it did in the first case seen by Gross and his associates. In our case, as in 2 of the 3 previously reported, there were anomalies of the vertebral column.

In the present case, there was no question as to the appropriate surgical approach. Fortunately, the entire cyst could be excised from the right thoracotomy approach although a portion of the stalk was left behind. As Gross, Neuhauser, and Longino have pointed out, when symptoms are due to compression of the thoracic structures, thoracotomy and excision of the intrathoracic portion of the intestinal diverticulum alone will suffice. When, however, symptoms are due to acid-peptic digestion with inflammation, ulceration, and hemorrhage, excision of the entire anomalous structure is advisable. As illustrated in Case 3 reported by Gross and co-workers, and by our current report, even in these instances, right thoracotomy approach alone may suffice.

In cases presenting themselves during early infancy, we feel that operation should be restricted to thoracotomy alone. If an abdominal approach becomes necessary, it should be carried out at another operation.

The atelectatic lower lobe in this case, as in many cases of Bochdalek hernias in the newborn associated with fetal atelectasis, partially responded to continuous insufflation at the time of surgery and went on to complete expansion during the postoperative period.

SUMMARY

An additional case is reported of a diverticulum originating from the small intestine and traversing the right diaphragm to present in the right thorax as a large cystic mass which compressed the thoracic structures to produce symptoms of cough, respiratory difficulty, and cyanosis in a 3-week-old infant. Unlike the 3 previously reported cases in which the thoracic diverticulum was in open communication with the small intestine, in the present case the cystic lesion was attached to the small intestine in the region of the retroperitoneal duodenum by means of a blind stalk. Operative approach was by right thoracotomy. The cyst was found to have produced total atelectasis of the right lower lobe. Fortunately, the entire cyst, together with its subdiaphragmatic extension and a portion of the stalk, could be excised from the thoracotomy approach, thereby averting the possibility of a secondary abdominal operation.

This anomaly is essentially an intestinal duplication which retains connection, either open or closed, with its point of origin from the small intestine but which is sequestered in the thorax by the formation of the diaphragm. It is another of the long list of anomalies producing serious symptomatology in infancy which, if recognized and appropriately extirpated at an early stage, is amenable to complete and brilliant cure. There have been no fatalities in the cases reported to date.

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